Official Journal of the Interstate Postgraduate Medical Association

Volume 23, Number 2 **FEBRUARY 1958**

Postgraduate Medicine

University of Colorado School of Medicine Special Issue

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References: (1) Jackson, G. G., & Grieble, H. G.: *Ann. New York Acad. Sc.* **69**:493, 1957. (2) Jones, W. F., & Finland, M.: *Ibid.* **69**:473, 1957. (3) Lepper, M. H.; Simon, A. J., & Marienfeld, C. J.: *Ibid.* **69**:485, 1957. (4) Ross, S.; Ahrens, C. E., & Zaremba, E. A.: *Ibid.* **69**:501, 1957. (5) Walker, W. F., & Hamburger, M.: *Ibid.* **69**:509, 1957.

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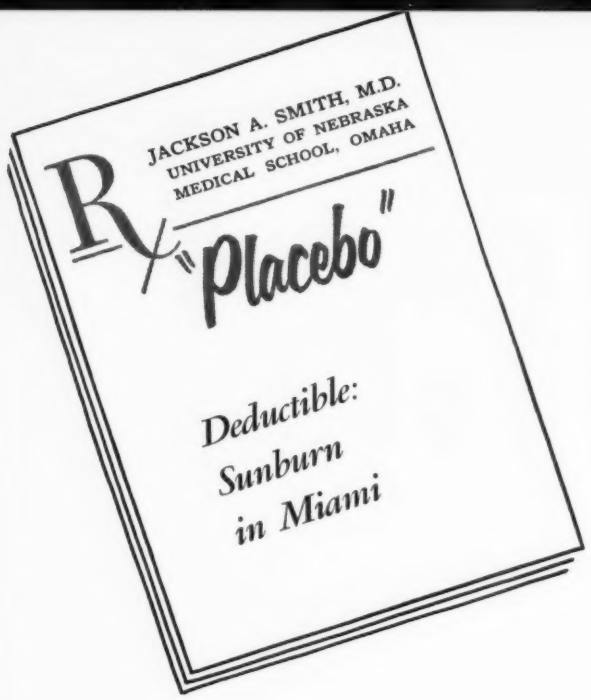

AFTER taking the only first-class flight from Chicago to Miami (with an hour's stop in Atlanta) the change in climate is obvious—it's hot—but the hotel is so well air-conditioned you think you're back in Chicago.

This particular luxury flight included free cocktails (you pay for the whiskey but there's no charge for using the glasses, the ice or the muddler), no free gum (but the stewardess will hold your nose while you pop your ears), and plenty of chances to practice the "outhouse quick step" while you try to guess which lavatory might be empty. Personally, I prefer to rough it on United's nonluxury flights, with free gum, grapes, cheese and indicator lights on the lavatories; they even have a "prayer rug" for the nervous group on their long flights, and sarsaparillas are on the house.

While waiting for the luggage, I leafed through a couple of news magazines to see which ancient maladies had been wiped out during the week. One of the better articles was titled "How I 'kicked the habit' after 10 years on a tranquilizer." I was also happy to find that a new ataractic had been synthesized; the formula is CH_3OH, and it is marketed under the trade name "Old Ulcer"—it provides a sort of burning calm. They say its emetic effects are twice those of any previous tranquilizer. The only side effects are seen at conventions when taken in higher doses, and they include a parkinsonianlike gait, with a tendency to drool and a masklike facies.

You can see every kind of fur on a lady's back in Miami, from a weary weasel to a hairy mole (better try that again; "mole, i.e., a fur-bearing insectivore with minute eyes, concealed ears and soft fur," found only in dark places such as night clubs, bars and airport limousines). Not wanting my wife to be embarrassed for lack of a stole, before we left home I went right out and—borrowed one from a neighbor.

We stayed in a small, adequate hotel with a conservative financial plan. It was one of the older hotels; they built it two seasons ago. The service was excellent and the room was comfortable, but the view of the ocean wasn't so good—it was on the wrong side.

You just don't find rooming houses in other parts of the country like those in Miami Beach; they all look like the Taj Mahal with elevators. In fact, you could hardly find a better place for a picnic than in their lobbies; they have everything from running water to shade trees.

All the larger hotels have night clubs, but not being too familiar with local customs, it seemed wise to inquire what the going rates were before ordering a hamburger. Having an Oriental disdain for discussing money, I tactfully asked, "How much?"

The head waiter looked as though he'd seen a bug on a salad and replied, "We only have a minimum charge, sir."

"And what might that be?" I asked, remembering the lobby and wanting no part of the fourth mortgage.

"Relax," he answered, "you're safe—it's off season."

Feeling as secure as a decoy on a game warden's pond, I waved him on.

"I believe I can find you a table," he confided, extending his arm, palm up.

This was quite an accomplishment since the room only seated 800 and there were more in the band than in the audience. Entering into the spirit of things, on our way to the table I crossed his still upturned palm with silver (someone had dropped a fork and I handed it to him).

The return flight was uneventful. We flew around over Chicago a while, then landed in Indianapolis, but still made it back to Nebraska in time for the first blizzard.

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Riker LOS ANGELES

Your Questions answered

Readers may send questions from their own practice or other medical problems which will be answered by qualified consultants. Replies are forwarded by mail immediately and selected questions and answers are published each month in this section.

• URINARY INCONTINENCE FOLLOWING OPERATION

Q. Using Millin's method, I have operated on two patients who had adenoma of the prostate. Following the operation, they had urinary incontinence. Can you explain this? Since the operative procedure was performed without difficulty and with no deviation from the technic, I am anxious to know what could have happened. I would appreciate recommendations for treatment.

M.D.—Greece

A. Most cases of incontinence that I have observed have occurred after vertical incision of the capsule, in which the muscle has been cut, injured or torn during surgery. These are not easy to correct. After sufficient time has elapsed, we have used the Marshall Marchetti technic; however, this has not always been successful and has been repeated in a few instances.

• VITAMIN K IN OBSTETRICS

Q. Would you please advise me of the current opinion on the routine use of vitamin K in obstetrics. Should it be given to the parturient mother, the infant, both or neither? If so, in what dosage and how often should it be given?

Would you also comment on the advisability of circumcision at the age of two or three days, with or without the use of vitamin K.

M.D.—Maine

A. Since it is very difficult or even impossible to decide beforehand which cases need the prophylactic administration of vitamin K for the control of prolonged prothrombin times and since prophylaxis is inexpensive and safe, it is generally recommended that vitamin K be administered routinely to all mothers just before or during labor or to their infants immediately after birth. There is ample evidence that a single 1 mg. dose of water-soluble vitamin K is adequate to prevent hemorrhagic disease in a newborn infant. This corresponds to 3 mg. of menadiol sodium diphosphate (SYNKAYVITE®).

At the institution with which I am associated, all the infants receive vitamin K prophylactically immediately after birth. Hence, there has been no experience with circumcision performed on the second or third day among infants who have not received vitamin K prophylactically.

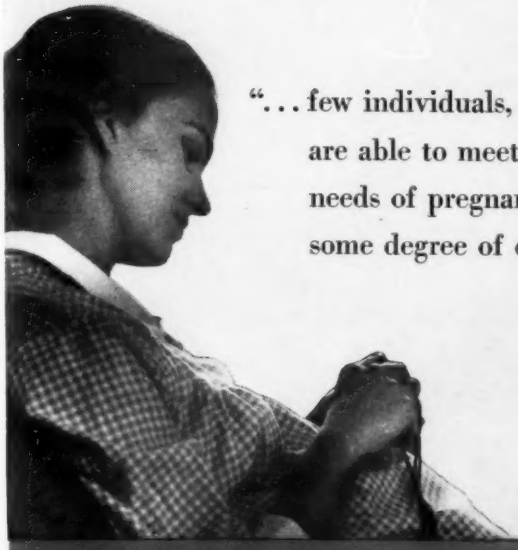
• ALBAMYCIN® IN CLOSTRIDIUM WELCHII INFECTION

Q. Is Albamycin effective in treating *Clostridium welchii* infection? I recently had a case of gas gangrene, which was only clinically diagnosed. Of the usual antibiotics, only Albamycin gave relief.

M.D.—Peru

A. In general, the spectrum of Albamycin antibacterial action is gram-positive organisms (*Clostridium*). Although the "usual antibiotics" are effective against most gram-positive bacteria, specific sensitivity tests should be performed for the organism involved to determine drug resistance. Apparently this organism was sensitive only to Albamycin (novobiocin).

(Continued on page A-24)



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Niacinamide	20 mg.
Calcium Pantothenate	5 mg.
Ascorbic Acid	75 mg.
Calcium, elemental (as calcium carbonate, 375 mg.)	150 mg.
Iron, elemental (as ferrous sulfate exsiccated, 33.6 mg.)	10 mg.
Iodine, elemental (as potassium iodide, 0.2 mg.)	0.15 mg.
Potassium (as the sulfate)	5 mg.
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Manganese (as the sulfate)	1 mg.
Zinc (as the sulfate)	1.5 mg.

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Reference: 1. Tompkins, W. T. in Wohl, M. G. and Goodhart, R. S.: *Modern Nutrition in Health and Disease*, Lea & Febiger, Philadelphia, 1955, p. 886.

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• POST-TRAUMATIC ATELECTASIS; TRAUMATIC RUPTURE OF TRACHEA AND BRONCHI

Q. I would like some information on post-traumatic atelectasis, clinical status and treatment; traumatic rupture of the trachea and of the bronchi and pulmonary parenchyma.

M.D.—Quebec

A. *Post-traumatic atelectasis, clinical status and treatment*—Post-traumatic atelectasis is quite common. In the conscious patient with not too severe an injury, relief of pain, preferably by injections of procaine into the intercostal nerves, will make it possible for the patient to cough and this will sometimes relieve the atelectasis. Nasal suction with a catheter which will provoke coughing and remove secretions is helpful for the patient who is not too severely injured. If these measures do not relieve the atelectasis, bronchoscopy and removal of the secretions are indicated.

In the severely injured patient or in those with multiple injuries, a tracheostomy should be done to provide a means of removing accumulated mucus or blood by suction and to decrease dead air space and to provide more tidal air.

Traumatic rupture of the trachea—If the trachea is ruptured, associated blood vessel damage is often fatal before treatment can be instituted. However, there are instances in which the trachea is fractured where survival time is sufficient for treating the lesion. The trachea may be ruptured either in the cervical portion or within the thorax. A direct blow on the neck may cause rupture in the cervical trachea, and crushing injuries of the chest may result in an intrathoracic fracture of the trachea.

In cervical injuries, a subcutaneous emphysema will develop rapidly, and tracheostomy should be performed immediately. As soon as the patient's condition stabilizes, the wound should be repaired. In patients in whom there has been a considerable loss of tissue, prosthesis has been employed. However, this has usually been done as a secondary operation after development of a stricture following the initial repair. Stainless steel mesh is probably the best type of prosthesis.

In traumatic rupture of the trachea within the thorax, the tear is usually just above the carina and frequently on the right side. A rapidly progressive tension pneumothorax will develop in these patients. The tension pneumothorax requires first consideration with decompression by an intercostal catheter and water-seal trap. Early operative repair is indicated as soon as the patient's condition permits surgical intervention. Prosthesis should be avoided. It is important that, in suturing the trachea, allowance be made for the largest possible lumen. To do this a longitudinal incision should be sutured transversely, employing the same principle as used in the intestine. In late cases with stricture formation, a prosthesis sometimes must be used. With proper early management, this complication should be avoided in the majority of cases.

Traumatic rupture of the bronchi and pulmonary parenchyma—Traumatic rupture of the large bronchi will produce a clinical picture almost identical to rupture of the trachea. A progressive tension pneumothorax and leakage of air into the mediastinum usually produce marked subcutaneous emphysema in the neck and mediastinal emphysema. The air leak may be small and, therefore, the subcutaneous emphysema may not form rapidly. Decompression of the progressive tension pneumothorax must be accomplished immediately, and, as soon as the patient's condition permits, primary repair of the defect should be done.

Some hint of a ruptured trachea or large bronchus may be gained if a progressive tension pneumothorax develops in association with subcutaneous and mediastinal emphysema but with minimal evidence of fractured ribs or hemothorax which would indicate a parenchymal tear.

Most small injuries to the pulmonary parenchyma can be treated by relieving the pneumothorax and by aspirating blood if an associated hemothorax is present. It is extremely rare that an emergency open thoracotomy is indicated.

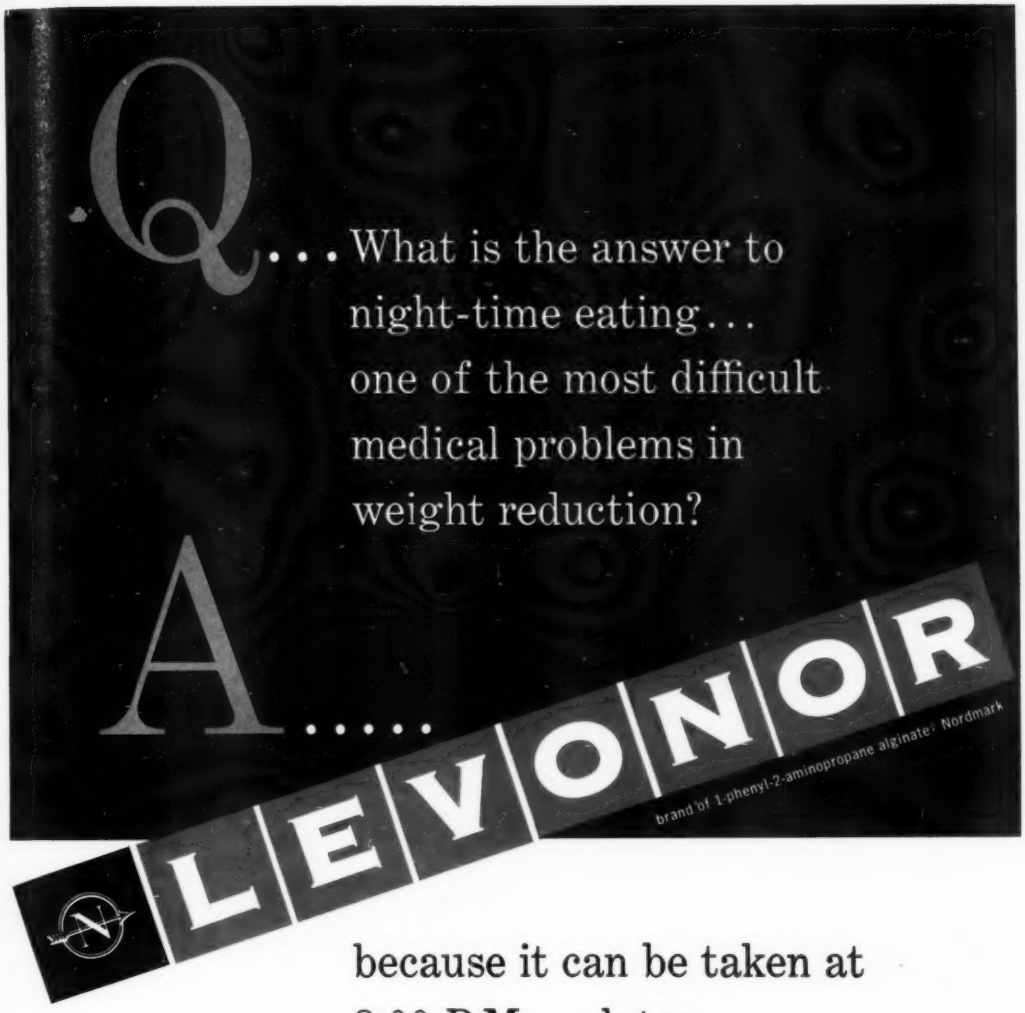
• WALNUT STAIN FOR VITILIGO

Q. In a recent issue there was an inquiry regarding the use of walnut stain as a mask for vitiligo. I have been unable to obtain the stain. Where can it be procured?

M.D.—Alabama

A. The best method for preparing walnut stain is to crush the hulls of black walnuts and soak them in acetone for 48 hours. The solution must be kept tightly corked and away from flames. This extract makes a nice stain to paint on vitiliginous lesions.

(Continued on page A-26)


Q
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1. Sc. Exhibit, N. Y. State Med. Meeting, Feb. 18-21, 1957.

†Patent Pending *Trademark

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• COLD STERILIZATION OF SYRINGES

Q. Is there an adequate method for cold sterilization of syringes used for intramuscular and subcutaneous injections?

M.D.—Wyoming

A. No. Syringes and needles should be placed in large, plugged test tubes or wrapped in cloth and sterilized by baking with dry heat or by autoclaving.

Another satisfactory method is to sterilize syringes and needles in boiling water in a small pan just before use.

• AMYOTROPHIC LATERAL SCLEROSIS

Q. The diagnosis of amyotrophic lateral sclerosis was recently made in one of my patients, a 42 year old man with involvement of the muscles of the left shoulder, arm and hand, and slight involvement of the muscles of the right shoulder girdle.

The standard textbooks do not mention any effective form of treatment. Have there been any recent developments in this field?

M.D.—Ontario

A. The treatment of amyotrophic lateral sclerosis continues to be most unsatisfactory. The patient should be advised to avoid both fatigue and specific strengthening exercises. If he has symptoms of bulbar involvement, advice in maintaining adequate nutrition through the use of a high caloric, high vitamin, soft or liquid diet may be indicated. In certain patients, the problem of tracheotomy and gastrotomy may be considered. In several patients, neostigmine given in small doses has seemed to be helpful symptomatically, although it does not in any way alter the course of the disease.

Various specific therapies have been suggested. In one series, a number of patients received whole, raw gastric mucosa, cortisone preparations, vitamin E, vitamin B_{12} and calcium disodium versenate, all of which have been reported useful in the treatment of this condition. The therapeutic results of all these agents were monotonously the same. In every instance, many, if not all, of the patients reported after a month or two of each treatment that they showed remarkable improvement; whereas, objective testing has revealed the expected progression of the disease.

(Continued on page A-28)

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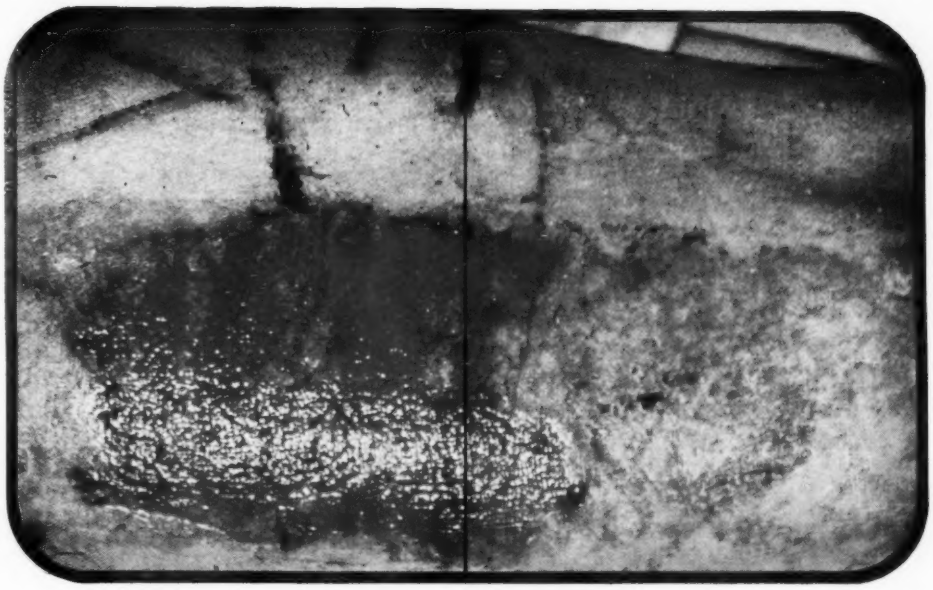

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Jeffords, J. V., and Hagerty, R. F.: Ann. Surg. *145*:169, 1957.

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• NEPHROPEXY

Q. In the actual advances in surgery, what is the place of "nephropexy"? In nephroptosis, is surgical intervention the right procedure? Are the results good throughout the patient's lifetime? If so, what kind of operation is best?

M.D.—Belgian Congo

A. "Nephropexy" is usually done to replace the kidney in a high position when ureteropelvic obstruction is present and needs correcting by plastic surgery.

This operation is rarely done to correct low position of the kidney unless pain is present, slow or delayed emptying of the kidney is demonstrated without evidence of anatomic obstruction at the ureteropelvic junction, and no pathologic evidence can be found in adjacent organs or tissues that could produce pain.

When no obstruction is present at the ureteropelvic juncture and nephropexy is done only for the position of the kidney, the results are not good. Only a small percentage of patients get relief from the symptoms. Any operation is satisfactory that holds the kidney in good position so that the flow of urine through the ureteropelvic juncture is direct and entirely downward toward the bladder. To produce this direct drainage, the upper pole of the kidney is usually placed toward the spine with the lower pole outward. Nonabsorbable material should be used to fix the kidney. The "Deming" technic, which is popular now, is a good one to use.

• HORMONE THERAPY IN HABITUAL ABORTION

Q. What is the present status of hormone therapy in the treatment of habitual abortion? If it is impractical to give progesterone intramuscularly, is there any value in prescribing oral progesterone? If so, what is the dosage and when should the drug be withdrawn?

M.D.—Newfoundland

A. The current vogue in endocrine therapy of habitual abortion is progesterone. If it cannot be given intramuscularly once a week as 250 mg. of DELALUTIN®, it may be administered orally as NORLUTIN® in a dosage of 5 mg. four times a day (20 mg. per day). Progesterone should be administered through the fifth month of gestation.

(Continued on page A-30)

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for freedom from fear
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SUPPLIED:

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• ERYTHEMA MULTIFORME

Q. In the last two years, a 20 year old man who works as a machinist has had several attacks of erythema multiforme. There is no family history of allergy. During the last two attacks, the patient has been treated with CYCLOTROPIN® without effect. He also has been given 20 units of achton prolg. (*sic*) and 10 mg. of prednisone daily without result. As this patient works primarily on ships sailing from here, is there any remedy which he might use if he has an attack while he is away?

M.D.—Denmark

A. The cause of erythema multiforme is not known. In some cases, recurrences are preceded by an attack of herpes simplex or streptococcal sore throat. In the latter instance, the course of the disease may be altered by the prompt administration of suitable antibiotic agents. In the symptomatic treatment of erythema multiforme, salicylates often are effective. If steroids are used, they must be given judiciously, and the doses must be regulated according to the need of the individual. Occasionally, the administration of ACTH by intravenous infusion early in the course of the condition will abort the symptoms. If 10 mg. prednisone given daily has not been effective, the dosage may be increased to 30 or 40 mg. for the first two or three days; however, considering the average medical control available on ships, it may not be wise to recommend such procedures.

• INJECTION TREATMENT OF HEMORRHOIDS

Q. I would appreciate the most recent information available on the treatment of hemorrhoids by injection. What preparations are used in this type of treatment; what kind of syringes and needles are needed?

Would you also recommend a recent textbook on the treatment of hemorrhoids?

M.D.—New York

A. In order to be treated by injection, hemorrhoids should be small, internal and uncomplicated, with bleeding in small amounts the chief symptom. Hemorrhoids which are large, accompanied by large externals or other anorectal pathology, or which produce symptoms such as protrusion, should not be treated by injection unless the patient's general condition contraindicates adequate surgery. Such patients should be warned that treatment by injection will bring improvement but not complete satisfaction.

Two main preparations are used in injection treatment. These are a 3 to 5 per cent solution of phenol in almond oil and a 5 per cent aqueous solution of quinine and urea hydrochloride. The latter is easier to administer, can be used in smaller quantities, and is generally much more satisfactory. The only contraindication is sensitivity of quinine.

It is possible to give adequate injections of quinine and urea hydrochloride using an ordinary tuberculin syringe and a ½ in. 28 gauge needle. The hemorrhoid is exposed through a suitable speculum, its upper pole wiped dry with a cotton applicator and then swabbed with an antiseptic such as an aqueous solution of 1:100 ZEPHIRAN® chloride. The needle is inserted into the upper pole of the hemorrhoid, the plunger withdrawn in order to be sure that the needle is not in a vein, and 0.25 to 1 cc. of solution is injected. The needle and anoscope are withdrawn in one motion.

In order to give injections with the phenol-in-oil mixture, a large-bore needle with a bayonet attachment is necessary; this is attached to a 2 to 5 cc. syringe. The injection is given in the submucosa above the upper pole of each hemorrhoid in amounts of 1 to 2.5 cc., that is, until slight bulging can be seen. The overlying mucosa should not be blanched. One hemorrhoid is injected at a time and a minimum of three days should elapse between injections.

It should be noted that injections of hemorrhoids must be perivenous and not intravenous. Properly performed, the treatment is entirely painless. Complications are quinine sensitivity reactions and slough; the latter develops after a period of several days and may produce dangerous hemorrhage.

The subject is well discussed in "Proctology," by Bacon, Ross and Recio, J. B. Lippincott and Company, 1956.

• VITAMIN E AND MULTIPLE SCLEROSIS

Q. What is your opinion on the role of vitamin E in multiple sclerosis?

M.D.—Montana

A. There is no substantial evidence that vitamin E plays any role in the production, prevention or evolution of multiple sclerosis.

What's happening in Medicine ?

POSTGRADUATE MEDICINE'S REPORT of late news of interest to practicing physicians

MENTAL HOSPITAL "ALUMNI" ASSOCIATION URGED

American Association for the Advancement of Science, Indianapolis:

- Former mental patients should not try to forget their hospital experience as a bad nightmare. The mental hospital curriculum is potentially an extremely enriching experience which should be integrated with the rest of life. Patients should form "alumni" associations to give to the hospital as well as receive and to help other patients bridge the gap between responsible living in the community and the tradition of ordered dependency on the hospital.—Professor Temple Burling, Cornell University, Ithaca.
- All of medical history demonstrates that answers do not come unasked from the research laboratory. Observant physicians must pose the questions. A danger in independent basic research is the tendency to lose contact with medical reality. Clinical science, with its inherent vagueness and complexity, is frustrating, but it is the only possible approach to medical problems.—Dr. William B. Bean, State University of Iowa, Iowa City.
- Growth can be limited by its inhibitory products. An attempt should be made to collect products of a cancer, concentrate them, and use them back on the cancer.—Professor S. Meryl Rose, University of Illinois, Champaign.

FLUORINE CITED AS DIETARY ESSENTIAL

Symposium on physiology and pharmacology of fluorine, A.A.A.S., Indianapolis:

- As a result of its proved effect on resistance to dental caries, fluorine must be classified as an essential dietary factor in the same way that many other nutrients are essential for promoting optimal health in behalf of a single physiologic body function. Future studies may well broaden our concept of "essentiality" to include other effects not yet understood. For example, only recently has it been possible to demonstrate that fluorine is present in various soft tissues of the body, such as the heart and kidneys, although its function in these tissues is not yet known.—Joseph C. Muhler, D.D.S., Indiana University, Indianapolis.
- One continues to hear that fluorides increase the incidence of cardiovascular disease. Data in rat experiments, however, suggest that the use of fluorides, even at relatively high levels, is not associated with changes in cholesterol metabolism.—Dr. Wolfgang Buttner, Indiana University, Bloomington.
- An analysis of the 1940 and 1950 census years in five cities before and after controlled water fluoridation shows no significant difference in human mortality rates.—Thomas L. Hagan, D.D.S., U.S. Public Health Service, Washington, D.C.

WHY THE "DAREDEVIL"?

American Psychoanalytic Association, New York:

- The problem of people who risk their lives for a "thrill" has been examined through the analysis of a racing driver. It was concluded that the thrill results mainly from the excess of energy involved when the ego submits to oedipal desires and then is able to master them.—Dr. Samuel H. Lerner, Cleveland.
- Systematic investigation of hallucinatory experiences (predominantly auditory) in 10 schizophrenic patients revealed that the hallucinated objects are formerly loved persons who gratify instinctual needs and duplicate certain executant ego functions.—Dr. Arnold H. Modell, Brookline, Mass.
- There is evidence that from earliest life certain children are able to alter and influence their environment in such a way that the environment created by this early personality may itself be pathologic for future development. In this sense environmental factors often cannot be separated from constitutional ones.—Dr. Martin H. Orens, Great Neck, N.Y.

TRANSNASAL APPROACH FOR HYPOPHYSECTOMY

Beads of yttrium 90 are being implanted in the pituitary gland with a transnasal technic in about 30 minutes. The approach is deemed quicker, simpler and safer than through a flap in the skull. Since the technic has been in use less than a year, it is not yet possible to gauge its long-term effectiveness in treating far-advanced mammary cancer.—University of Chicago Cancer Research Foundation, Chicago.

DITHIAZANINE HITS INTESTINAL PARASITES

Fourth Bahamas medical conference, Nassau:

- Promising action against five species of intestinal helminths has been seen following use of dithiazanine. Broad-spectrum action has been achieved in 500 patients afflicted with trichuriasis, strongyloidiasis, ascariasis, enterobiasis and necatoriasis. More than 1,500,000,000 individuals in the world are infected with parasitic worms, many of which have heretofore resisted treatment.—Dr. William W. Frye, Louisiana State University, New Orleans.
- When taken by mouth from the fifth to the twenty-fifth day of the menstrual cycle, progestins prevent the formation of an ovum in human females. In a group of several hundred volunteers in Puerto Rico, there were no pregnancies among those who took the tablets regularly.—Dr. Gregory Pincus, Worcester Foundation for Experimental Biology, Shrewsbury, Mass.

KWASHIORKOR NOW A U.S. DISEASE

Sixteenth annual meeting of the American Academy of Dermatology and Syphilology:

- The protein deficiency disease, kwashiorkor, first observed in equatorial Africa and since reported in parts of Asia, Europe and Central and South America, has now spread to the United States. The first four cases, all involving Negro girls ranging in age from 20 months to 11 years, have been detected. Symptoms include vomiting, abdominal distention, peeling skin, mental apathy, diarrhea and cold extremities. All four responded to high protein therapy.—Dr. V. Medd Henington, Louisiana State University, New Orleans.
- Fourteen cases of dermatitis caused by mites in pigeon nests have been treated. When pigeons are absent from their nests, mites will quickly transfer to an emergency host such as man. Reactions vary in intensity from a mosquito bitelike lesion to a generalized toxic eruption accompanied by malaise and fever.—Dr. Gerard A. DeOreo, Western Reserve University, Cleveland.

CLINICAL COLLOQUY

My patients complain that the pain tablets I prescribe are too slow-acting... they usually take about 30 to 40 minutes to work.

Why don't you try the new analgesic that gives faster, longer-lasting pain relief?

What is it... how fast does it act?

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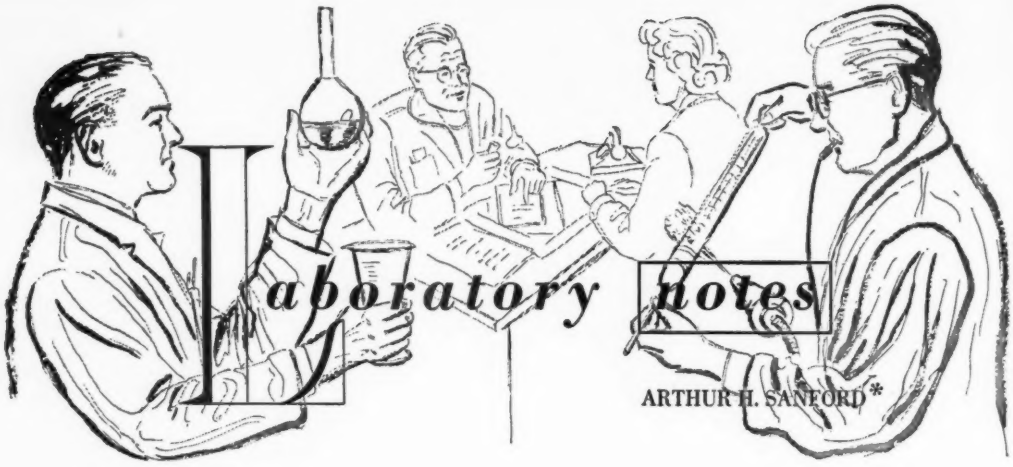

ARTHUR H. SANFORD*

Fluid Balance

RECENTLY, it was my privilege to review a monograph[1] on fluid balance for POSTGRADUATE MEDICINE. The author is director of blood transfusion service and a lecturer in hematology in the University of Bristol, England. This small book is packed with terse suggestions that are helpful to laboratory workers acting as consultants. It also is valuable for clinicians who do not have laboratory facilities available to aid in the care of patients in whom it is necessary to maintain a body fluid equilibrium.

It is impossible, of course, to cover this important subject in a column. However, I would like to point out a few of the interesting discussions contained in this monograph.

The concise summary of daily water requirements shown in table 1 is worthy of study.

In various conditions, particularly after surgery or trauma, sodium chloride may be retained, with little excreted in the urine. To determine urinary chloride, the author suggests use of the simple Fantus test.[2] The reagents required are 20 per cent potassium chromate solution and 2.9 per cent silver nitrate solution. A scrupulously clean dropping pipet and a test tube are the only equipment necessary for the test. Place 10 drops of freshly collected urine in a test tube. Rinse the pipet well with distilled water and add 1 drop of 20 per cent potassium chromate solution. Rinse the pipet and add 2.9 per cent silver nitrate solu-

TABLE 1[1]

SUMMARY OF DAILY WATER REQUIREMENTS

ROUTE OF LOSS	DAILY AVERAGE *(ml.)*	INCREASE BY 500 ML.	INCREASE BY 1000 ML.	ADDITIONAL REQUIREMENTS
Skin and lungs	1000	Temperature 101° F., especially if respirations increased	Marked visible sweating	
Urine	1000	Fevers, protein catabolism, etc.	Impaired renal concentrating power (fixed low specific gravity)	Replace water lost in alimentary tract secretions volume for volume (vomiting, diarrhea, fistulas, etc.)
Total water which may be required to cover insensible and urinary loss	2000	2500 to 3000 ml.	3000 to 4000 ml.	

*Emeritus Staff, Section of Clinical Pathology, Mayo Clinic; Director of Laboratories, Rochester State Hospital, Rochester, Minnesota.

(Continued on page A-40)

INTRODUCING

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High in protein, low in cost, and—when reconstituted—with only half the calories of whole milk, new PET *Instant* meets the needs of the physician in many special-diet cases.

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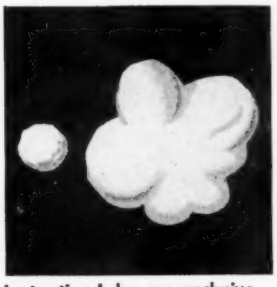

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Appetizing flavor. Never powdery or watery—always deliciously fresh tasting.

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NONFAT DRY MILK

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TABLE 2[1]

DAILY SALT REPLACEMENT

TO REPLACE	LABORATORY FACILITIES AVAILABLE	LABORATORY FACILITIES NOT AVAILABLE
Basic requirement	Calculate from quantitative examination of urine	Allow 78 mEq. Na; 78 mEq. Cl (i.e., 4.5 gm. NaCl) or according to Fantus' urine examination. Omit during first 48 hours postoperatively, or replace according to Fantus' test
Visible sweating	Allow 50 mEq. Na; 50 mEq. Cl (i.e., 3 gm. NaCl) per liter	Allow 50 mEq. Na; 50 mEq. Cl (i.e., 3 gm. NaCl) per liter
Gastrointestinal secretions	Calculate from quantitative examination of losses by aspiration, fistulas, diarrhea	(1) Allow 155 mEq. Na; 155 mEq. Cl per liter (i.e., 9 gm. NaCl [normal saline]) or according to Fantus' test. (2) Test by litmus; if alkaline, replace by Hartmann's solution or by saline plus lactate or bicarbonate

TABLE 3[2]

COMPARISON OF PRINCIPAL FINDINGS IN PREDOMINANTLY WATER AND PREDOMINANTLY SODIUM DEPLETION

	WATER DEPLETION	SODIUM DEPLETION
History	*Impaired Intake*	*Loss of Secretions*
Clinical features		
Thirst	Present	Absent
Mucous membranes	Dry	Moist
Skin	May become flushed	Increasing pallor
Cramps	None	May be present
Blood pressure	Normal until late	Early fall, rapidly becoming profound
Urine examination	Usually oliguria. Sodium and chloride ions present	Normal volume at first. Sodium and chloride ions usually low or absent
Blood electrolytes		
Sodium	More than 145 mEq. per liter	Less than 135 mEq. per liter
Chloride	More than 105 mEq. per liter	Less than 98 mEq. per liter
Chloride and bicarbonate	More than 132 mEq. per liter	Less than 122 mEq. per liter
Hemoconcentration	Hemoglobin and plasma protein concentration normal until late	Hemoglobin above 100 per cent (14.8 gm.) and plasma proteins greater than 7.5 gm. (18 mEq. per liter) unless anemia or hypoproteinemia present
Plasma volume	Normal until late	Reduced early

tion drop by drop, shaking the tube well after adding each drop. Count the number of drops of silver nitrate required to change the mixture from yellow to brown. The number of drops signifies the number of grams of sodium chloride per liter of urine. Multiply by 17 to express milliequivalents of chloride. If there is no chloride present, the color will change with the first drop of silver nitrate.

The replacement of fluids and salt must be carefully controlled. Table 2 presents interesting information concerning salt replacement.

The comparison of findings in water and in sodium depletion given in table 3 is of interest.

Various conditions in which a careful consideration of fluid balance is important are presented clearly by the author.

REFERENCES

1. TOVEY, G. H.: Technique of Fluid Balance. Springfield, Illinois. Charles C Thomas, 1957.
2. *Ibid.*, p. 93.

patients of all ages benefit from

Peri-Colace

peristaltic stimulant—stool softener, Mead Johnson

Capsules • Syrup

softens stools and stimulates peristalsis

When bowel motility is inadequate ...defecation infrequent... Peri-Colace combines the stool-softener Colace with a new, mild peristaltic stimulant, Peristim (standardized preparation of anthraquinone derivatives from cascara sagrada). Because Colace keeps the stool soft, only a small amount of stimulant is needed. Action is gentle—usually in 8 to 12 hours—and side effects are minimized.

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COS76

Medicine from Abroad

FROM POSTGRADUATE MEDICINE'S CORRESPONDENTS

ENGLAND

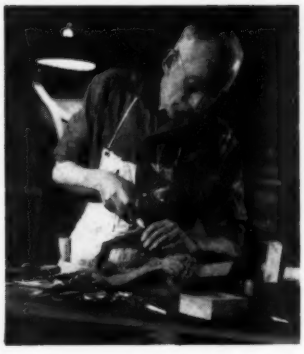
Aspirin and diabetes—It has been observed that salicylate has prevented diabetes, and that rheumatic fever and diabetes rarely coexist. An opportunity to investigate this unusual combination of disease was provided recently at the Western Infirmary, Glasgow, by a young male diabetic patient known to take insulin, who was receiving full salicylate treatment for acute rheumatism when admitted to the hospital. Dr. James Reid and Dr. A. I. Macdougall, with the technical help of Mr. M. M. Andrews, B.Sc. (a member of the Chemotherapeutic Unit of the Medical Research Council), then investigated the effect of aspirin in another seven diabetic patients as reported recently in the *British Medical Journal*. Each patient was given a constant low carbohydrate diet throughout the whole investigation. To establish the effect of diet alone, this regimen was begun about two weeks before aspirin administration. An intensive course of aspirin controlled by serum salicylate estimations was given to each patient for 10 to 14 days, with doses of 1 to 1.6 gm. being administered every four hours, omitting one dose in the middle of the night.

Aspirin was found to have a definite beneficial effect on the blood sugar, glycosuria and ketone excretion in diabetes of mild to moderate severity. The clinical symptoms of the disease, such as thirst, polyuria and pruritus, which are intimately related to the high blood sugar and glycosuria, were completely relieved by the drug. While it would be premature to suggest that aspirin might regain a place in the treatment of diabetes mellitus, if there is a genuine need for an oral compound to control diabetes, aspirin has an obvious advantage over the sulfonylureas because it may be given for prolonged periods without risk of agranulocytosis. Another point in its favor is that maximal tolerated doses lower the fasting blood sugar to normal without inducing hypoglycemia. The place of aspirin in the treatment of diabetes will, however, require further investigation, and in the last resort will depend on how well therapy can be controlled.

Mouth breathing—A discussion on this subject was opened by Mr. E. Gwynne-Evans, surgeon in charge of an upper respiratory diseases clinic at a children's hospital, at a recent meeting of the Section of Pediatrics of the Royal Society of Medicine. He has observed that nasal breathing depends on both the patency of the nasal passages and the efficiency of the oropharyngeal musculature. Failure of the oropharyngeal muscles is a more common cause of mouth breathing in children than is nasal obstruction due to enlargement of the adenoids. Of the various types of nasal obstruction, Mr. Evans thinks that swelling of the anterior nasal mucosa from allergic vasomotor rhinitis also is a more frequent cause in children than adenoidal enlargement. In infants and young children, a strong natural instinct toward nasal breathing prevails, and, pro-

(Continued on page A-52)

WORKING



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ARTHRITIC patients on STERANE can achieve a manual dexterity, dramatic in degree—frequently after salicylates and/or previous corticoids have proved unsatisfactory —with minimal incidence of electrolyte imbalance.

White, scored 5 mg. tablets (bottles of 20 and 100); pink, scored 1 mg. tablets (bottles of 100).

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viding that serious degrees of nasal obstruction are excluded—or corrected—the propensity to nasal breathing tends to overcome failure of the oropharyngeal muscles. He is quite certain that in the vast majority of children with so-called adenoid facies the adenoids are not at fault. These children with long faces, protruding upper teeth, receding chins, and apparently vacant expressions do not suffer from nasal obstruction, nor are they mentally dull, nor will they develop any permanent nasal, facial or oral deformities. Their facies is a normal type of natural physiognomy related to hereditary factors rather than to any structural defects.

Dr. C. F. Ballard, professor of orthodontics at London University, agreed that mouth breathing never results in oral deformities or leads to the production of adenoid facies. He is convinced that this facies is a normal phase in the development of a certain type of child and that it is probably an ectomorphic characteristic. The facies is uninfluenced by any type of remedial exercise or oral appliance. Orthodontic treatment may be necessary later, but usually not until the child is around 12 years of age. The majority of children with adenoid facies will eventually grow out of it.

Combined prophylactics in children—It is well known that the response to a primary dose or course of fluid toxoid may be significantly increased by admixture with a vaccine—for example, pertussis vaccine and diphtheria toxoid, or typhoid vaccine and tetanus toxoid. Moreover, it has been found that the addition of diphtheria and tetanus toxoids to pertussis vaccine did not have an adverse effect on the immunity response to injections of the mixture as compared with results obtained when the plain vaccine was used. But little is known of the effect on the response to the diphtheria toxoid of variations in the ratio of vaccine to toxoid in children, and even less with respect to triple mixtures.

Dr. Guy Bousfield, the London immunization specialist, and Dr. L. B. Holt of the Wright-Fleming Institute, London, have therefore investigated (Brit. M. J., November 23, page 1213) over a period of two years a series of cases of children less than two years of age, all originally Schick-positive. Immunization against whooping cough cannot reasonably be withheld in the very early months of life, because it is then that pertussis is most dangerous to the child, and this consideration certainly outweighs the very small risk of provoking paralytic poliomyelitis. The measure of the increase in risk entailed by adding fluid toxoid to the vaccine is still not precisely known, but the long-term risk in a severe falling-off in the immunization rate against diphtheria is one to be taken seriously. There would not seem to be any reason for not using mixed fluid tetanus and diphtheria toxoids in place of diphtheria toxoid only. Every effort should be made to encourage immunization of children against tetanus in order to avoid the several disadvantages attending the utilization of tetanus antitoxin.

The authors found that the addition of pertussis vaccine to diphtheria toxoid enhanced the Schick conversion rate progressively with increase of the dose of vaccine. The addition of purified tetanus toxoid to the constant amount of diphtheria toxoid also increased the Schick conversion rate. The addition of tetanus toxoid to a diphtheria toxoid-pertussis mixture resulted in a significantly lower Schick conversion rate than that obtained without tetanus toxoid. It was calculated that the addition of pertussis vaccine increased the antitoxin response to the diphtheria toxoid some 14 times, and that the further addition of tetanus toxoid to the mixture reduced that increment to about fivefold. The order of mixing the components of the triple prophylactic produced no difference in the conversion rate.

Drug penetration into cerebrospinal fluid—At a recent meeting of the Section of Experimental Medicine and Therapeutics of the Royal Society of Medicine, Dr. Honor V. Smith of Oxford pointed out that certain substances normally present in blood, or artificially introduced into the blood stream, either do not appear in the cerebrospinal fluid or do so only in minute quantities; this has an important bearing on both the pathogenesis and treatment of certain neurologic diseases. When the meninges are normal, none of the usual chemotherapeutic agents except the sulfonamides and isonicotinic acid hydrazide (I.N.A.H.) will enter the cerebrospinal fluid in anything except negligible quantities. However, it is widely held that inflammation of the meninges greatly increases the permeability of the barrier, but this important assumption requires careful verification. Not only does the effect on the barrier vary with the cause of the inflammation, but the effect of a given inflammation is not necessarily the same for all substances.

With regard to penicillin, the increase in penetration during the first phase of the reac-

(Continued on page A-54)

In urinary-tract infections

HIGH TISSUE LEVELS

HIGH BLOOD LEVELS

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SUSPENSION TABLETS

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Triple Sulfonamides, Wyeth

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tion is often negligible, while during the second phase a considerable increase in penetration takes place. In Dr. Smith's experience the passage of penicillin from blood to cerebrospinal fluid is far too erratic to be depended on in the treatment of such a serious disease as purulent meningitis. The position with regard to streptomycin is rather different: Dr. Smith has frequently found from 5 to 15 units per cubic millimeter in the cerebrospinal fluid six hours after intramuscular injection of a gram of streptomycin. Yet it has been conclusively shown that the results obtained in the treatment of tuberculous meningitis with streptomycin alone are significantly better when both intrathecal and intramuscular injections are given than when the systemic route is used alone. It is often said that the advent of I.N.A.H. has made the intrathecal administration of streptomycin unnecessary. But before any one drug can be accounted effective in the treatment of any case of meningitis, it must be shown that in that particular infection that particular drug is capable of crossing the blood-cerebrospinal fluid barrier in therapeutic amounts. It must also be remembered that if cortisone is used in treatment, the effect may well be to restore the barrier at the very time when maximal penetration of the drug is most urgently required.

DENMARK

Treatment with meprobamate—In reply to an article which appeared recently on the habit-forming properties of meprobamate (Kodahl, T. and Andreassen, J.: Ugesk. laeger 113:1067, 1957), Dr. T. Jersild has reported on a series of 150 patients treated with this drug at the Western Hospital and Western Prison, Copenhagen. On the basis of his experience, he feels that many of the conclusions reached by Kodahl and Andreassen are unwarranted.

Although in several cases, for example, the treatment of patients with delirium tremens, he had to administer dosages of four tablets every two hours up to 16 tablets in 24 hours (6.4 gm.), he observed no serious side effects in his patients. Abrupt withdrawal, even after such a high dosage, has not in any case produced the convulsions reported by a few authors.

In the treatment of delirium tremens, the effect of meprobamate is beyond dispute. Patients who were previously treated for the same condition with barbiturates and who remained delirious for up to five days despite the barbiturate medication have responded to MILTOWN® within less than 24 hours.

Kodahl and Andreassen reported that a striking restlessness was observed in several patients on withdrawal of the drug, and a few begged to be allowed to continue receiving the preparation. Jersild feels this cannot reasonably be taken as proof of habituation. Some patients may even become "placebo addicts," and these patients show how difficult it is to assess addiction to a drug when using the criterion that the patient is begging for it. He has cited two cases from his own experience.

A patient with severe pain due to a slipped disk was admitted to be cured of meperidine addiction. She had been given six tablets of meprobamate daily and apparently had become dependent on the drug. When it was withdrawn, she asked for further treatment, but was given placebo tablets with equally good effect. Another patient who was nervous, crying and sleepless was given meprobamate without obtaining improvement; whereas, SUAVITIL® and Suavitil placebo had an excellent effect. However, several attempts at withdrawing the placebo caused striking restlessness, fits of weeping, and sleepless nights.

In support of their thesis, Kodahl and Andreassen cited the results observed by Lemere (A.M.A. Arch. Neurol. & Psychiat. 76:205, 1956), who used meprobamate in the treatment of 600 patients, a large proportion of whom were previously alcoholics. He reported that 13 of his patients themselves increased their usual dosage (three to four tablets of 400 mg. daily) to a dosage of excessive quantities. Several of them lay in bed in a bewildered state all day, some went about appearing to enjoy the intoxication, and one had a car accident. In a large proportion of the cases, he states that it was impossible to withdraw the drug abruptly as the patients became extremely restless; but there was no difficulty when the dosage was gradually decreased. In two instances, he observed typical epileptiform seizures when the drug was abruptly discontinued.

However, at the time of Lemere's article, Osinski (J.A.M.A. 163:489, 1957) reported he had treated 314 patients with meprobamate (26 of whom continued the medication for 3 to 15 months) without observing any form of habituation. On this basis he states, "I think it would

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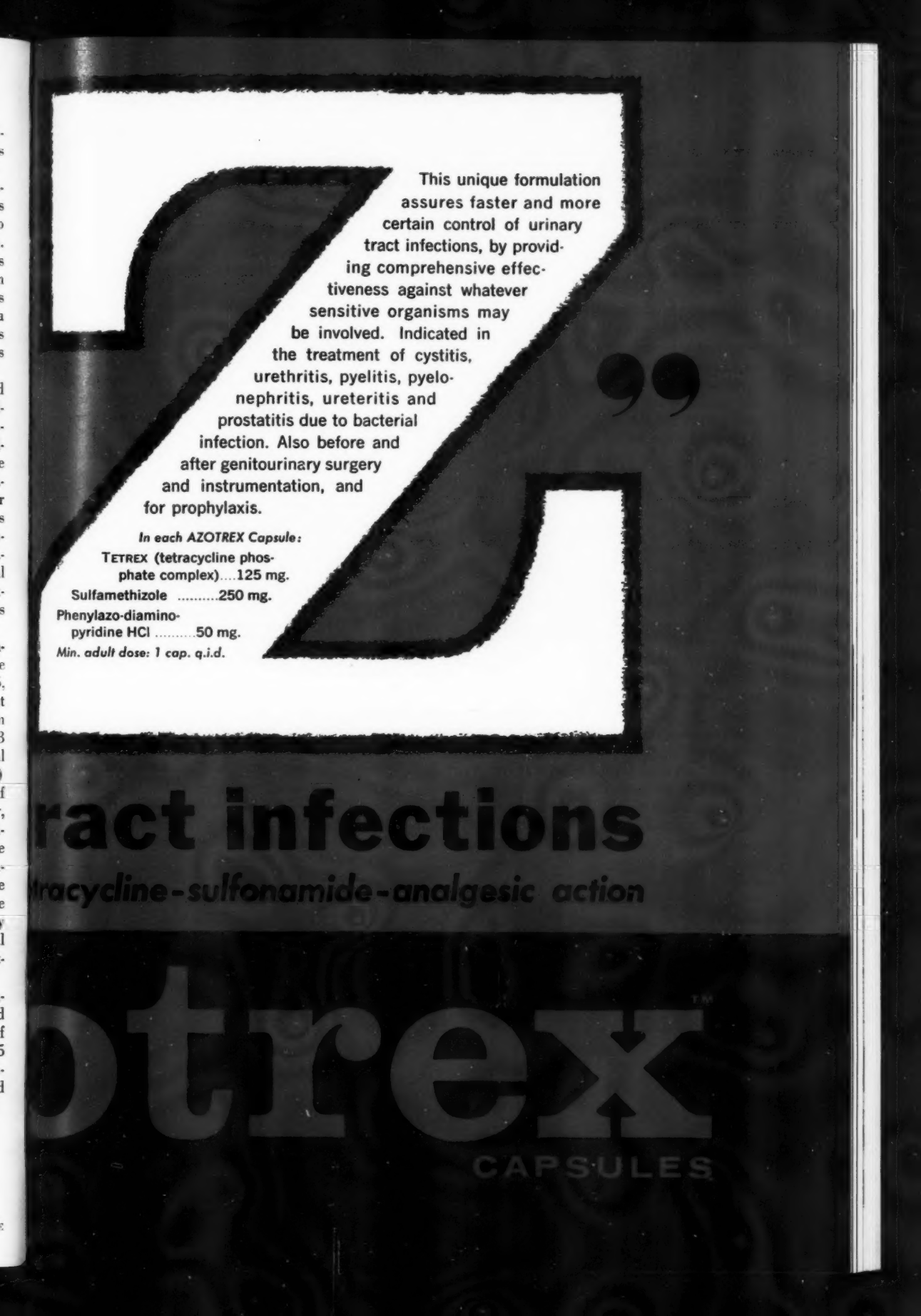
This unique formulation assures faster and more certain control of urinary tract infections, by providing comprehensive effectiveness against whatever sensitive organisms may be involved. Indicated in the treatment of cystitis, urethritis, pyelitis, pyelonephritis, ureteritis and prostatitis due to bacterial infection. Also before and after genitourinary surgery and instrumentation, and for prophylaxis.
In each AZOTREX Capsule:
TETREX (tetracycline phosphate complex)....125 mg.
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Min. adult dose: 1 cap. q.i.d.
ract infections
racycline-sulfonamide-analgesic action
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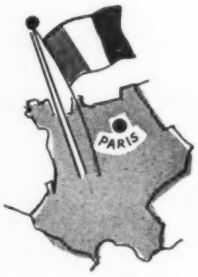
CAPSULES

be a pity if a drug as useful as meprobamate and as free of toxic reactions should acquire an undeserved reputation for habituation."

Since meprobamate tablets have been administered to literally millions of patients, Jersild feels it is somewhat farfetched to use as an example of the drug's harmful properties an isolated case (as cited by Lemere) in which a patient attributes his car accident to meprobamate medication. Jersild believes, on the contrary, that many accidents could be avoided if nervous, emotional drivers were given sensible treatment with meprobamate. In his opinion, Drs. Kodahl and Andreassen should have restricted themselves to the conclusion, "The time has not yet come to pass a final judgment on the tendency of meprobamate to cause addiction."

FRANCE



Etiology of diabetes mellitus—Professor Boulin (*La Presse médicale*), who organized one of the chief diabetic hospital services in Paris, believes that the prediabetic state begins in early childhood. Thirty per cent of diabetic cases are hereditary, and this figure increases to 50 per cent in infantile diabetes. Thirty per cent of children whose mothers have this disease become biologically diabetic, even though it remains below the clinical level, according to Priscilla White. It is assumed that the remaining 70 per cent of cases of diabetes are acquired, and that, without its cause being known, it appears in persons in their fifties. Many cases of diabetes either are not recognized or are ignored, especially in instances in which persons with the disease show no sugar in the urine. Frequently the level of blood sugar is normal in a fasting person. To prove that diabetes is present, a test must be performed which will provoke a high level of blood sugar exceeding 2 gm. after the ingestion of 50 gm. of glucose. Patients with such slight elevations in their blood sugar level will escape the hazards of acetoketosis and coma, but they are not immune to other complications of diabetes, such as ocular and cardiac complications, a high level of blood nitrogen, or a high level of blood cholesterol.

Preventive consultation for such persons, with the aid of this test, revealed 65 paradiabetics among 228 patients, or more than 28 per cent. More than a fourth of these patients with a family history of diabetes have the disease in latent form, but the majority will never be diabetic.

Professor Boulin stated that difficulty in the regulation of sugar from an early age ultimately is able to induce diabetes, and that the disease can be detected from the age of five. He suggested, therefore, that all children with a family history of diabetes (particularly when the mother is diabetic) should be tested annually after the age of five. At this age the condition is still curable, and early discovery will prevent the development of firmly established diabetes.

Abnormal concentration of sweat in mucoviscidosis or fibrocystic disease of the pancreas—Professor Julien Marie (Semaine hôp. Paris 31-38:592-600, 1957) employed a new technic in the study begun by Darling and di Sant'Agnese, who in 1953 showed that the secretion of sweat glands in cystic disease of the pancreas contains some electrolytes (particularly chlorine and sodium ions) in an abnormally high concentration. Characterized by cysts in the pancreas and in the lungs, by digestive and respiratory symptoms and hypotrophy, in children the disease is associated with intolerance to heat, as was proved by Kessler and Andersen in 1951. This abnormality is the result of excessive loss of electrolytes through perspiration. The high concentration of sweat (at least triple the normal values, or more than 100 mEq. per liter rather than 30 mEq.) is a constant phenomenon, independent of respiratory and digestive functional signs, and without any relationship to a possible insufficiency of the suprarenal glands. It is also present in atypical cases of mucoviscidosis, and since it occurs in other members of the sick child's family, it could well be hereditary.

The condition can be detected by various procedures. Perspiration is produced by raising the temperature of the room, by infrared rays directed at the patient, or by medicaments which induce sweating. Gochberg's theory on this condition states that exocrine sweat glands comprise a glomerulus that unduly concentrates the sweat, and a tubulus that reabsorbs the water at an increased rate. It is supposed that the cause of such overactivity is a hereditary and familial abnormality of the enzymatic system of these glands.

Professor Marie's technic is characterized by

(Continued on page A-60)

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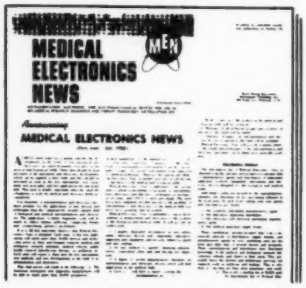

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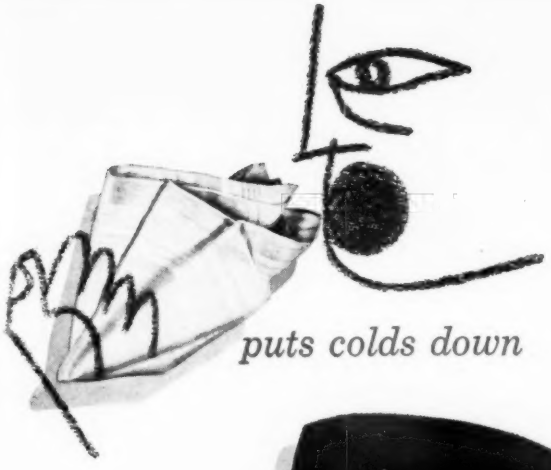
the large amount of collected perspiration, which permits easier analyses. The child is draped with a plastic sheet treated with silicon on one side; various precautions are taken to avoid an error due to feces or urine. One can easily observe the child through the transparent wrapping. He is kept in it from one to four hours, and when the drape is removed, the perspiration is gathered and put in large flasks. The error due to the presence of apocrine axillary perspiration and of the sweat from the palms and soles, which are richer in salts, is negligible. The method was well tolerated; some children reacted to it with an elevation in temperature to 38° C. for a short while. In 15 per cent of the cases, the amount of perspiration was very small, but it varied in other tests. Usually it is not possible to do this test on children less than three months of age.

Salazar and Souza, among other French authors, demonstrated that cases of mucoviscidosis are found among hypotrophic children, but other such children have a lesser degree of ionic concentration, generally ranging between 60 and 100 mEq. per liter. Patients with mucoviscidosis whose electrolyte concentration of perspiration is less than 60 mEq. are rare, and the diagnosis is more certain if it is more than 100 mEq.

The abnormal concentration of perspiration aids in the diagnosis of cases of atypical cystic fibrosis of the pancreas, which is important in preventing heat strokes in children.

Mental troubles and the Algerian events —There has not been any recrudescence of mental troubles in relation to the events in Algeria. Only a few exceptional cases of psychosis have been observed which were directly and unquestionably provoked by these events. A small number of psychoses seems to be closely related to some dramatic occurrence, but only in predisposed subjects and in those who had been sensitized. Their total number is not increasing, and the number of suicides perhaps has diminished. Explanations for these psychoses have been offered by Ably, who stated that the repetition of mental trauma produces a lowering in emotional receptivity; by Porot (*La Presse médicale*), who cited the mechanism of derivation, of induction, and of effective saturation by the conditions of real life which do not leave any space for free flowering of luxury; and by Ey and Cornavin, who stated that the psychosis fades away under the constraints of collective preoccupation which do not allow the unfolding of any egotistic delirious reaction.



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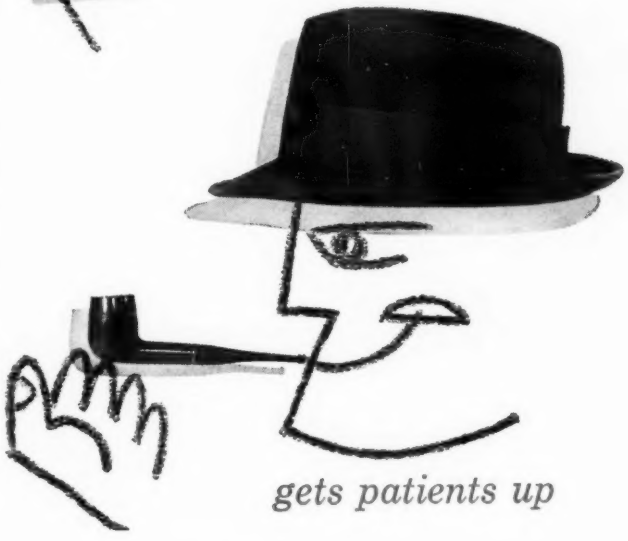

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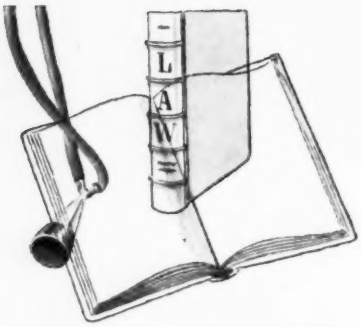

Forensic Medicine

Noninflammatory Findings in the Brain in Clinical and Forensic Medicine

OBSERVATIONS OVER A SIX YEAR PERIOD

SAMUEL A. LEVINSON

Louis A. Weiss Memorial Hospital, Chicago

THE purpose of this report is to discuss the pathologic changes in the central nervous system after death due to trauma to the head, changes that would serve as diagnostic criteria in distinguishing between traumatic and nontraumatic processes of the brain.

I shall compare the findings in two groups of cases. The first group consisted of cases referred to the coroner's office from Cook County Hospital* during a six year period. This hospital is a station for investigation of deaths due to trauma or allegedly due to trauma, and cases are referred to ascertain any causal relation between injury and death when there is a history of trauma to the head such as a fall while walking or during a fainting spell or a fall out of bed. The second group of cases were referred directly to the coroner's office. This group deals with similar disease processes of the brain associated with a definite history of trauma. In some instances death occurred immediately after injury to the head, while in others it was delayed for a short period.

Man tends to think that every effect necessarily presupposes a cause. In instances of injury to the head the cause-effect relationship has all too often been reduced simply to trauma-brain pathology. When death follows a penetrating injury of the skull and brain, trauma is quite clearly a bona fide cause, but in "closed" head injuries the causal inference cannot be isolated so precisely. From a medicolegal standpoint it is important to evaluate cases of trauma to the head critically in order to determine whether the injury was directly responsible for the pathologic findings in the central nervous system or whether the superimposed injury was the end result of pre-existing structural degeneration from continued pathologic-physiologic changes. For example, death of the cells may have caused the person to fall and thereby sustain a head injury.

Traumatic Brain Hemorrhage

The principal cause of traumatic brain hemorrhage is laceration of the brain associated with skull fracture. Occasionally one may observe cortical hemorrhages without evidence of skull frac-

(Continued on page A-68)

Presented before the International Meeting of Forensic Pathology, Brussels, Belgium, July 1957.

*Cook County Hospital in Chicago has 3,660 beds, and admissions number approximately 85,712 annually. Some 2000 deaths are investigated at the hospital per year. These include cases referred from the hospital proper, in which there is a history of trauma or alleged trauma or injury resulting from industrial hazards or noxious agents, as well as cases from the Cook County morgue. In about 60 per cent of these 2000 cases, investigation or autopsy reveals that death was due to natural causes. In about 40 per cent a traumatic cause is established. The 2000 cases investigated at the hospital represent a portion of the total of about 8000 cases, traumatic as well as nontraumatic, handled by the county coroner's office per year. Some 46,000 to 47,000 deaths are reported in Cook County annually.

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"Cardiac patients who show significant manifestations of anxiety should receive ataractic treatment as part of the therapeutic approach to the cardiac problem."[1]

1. Waldman, S., and Pelner, L.: Am. Pract. & Digest Treat. *8*:1075 (July) 1957.

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ture, as in contrecoup injury where areas of brain hemorrhage appear opposite the point of impact on the skull.[1] In contradistinction to cortical hemorrhage is hemorrhage in the basal ganglia. The latter is rarely the result of trauma although it may accompany trauma. Usually the history is that the person received a blow on the head or fell and struck his head, and later, at autopsy, hemorrhage in the basal ganglia is found. The hemorrhage may be interpreted as the result of the basilar fracture of the skull with lacerations of the brain. Conversely one may argue that the hemorrhage in the basal ganglia occasioned the loss of control and the subsequent fall which produced the skull fracture.

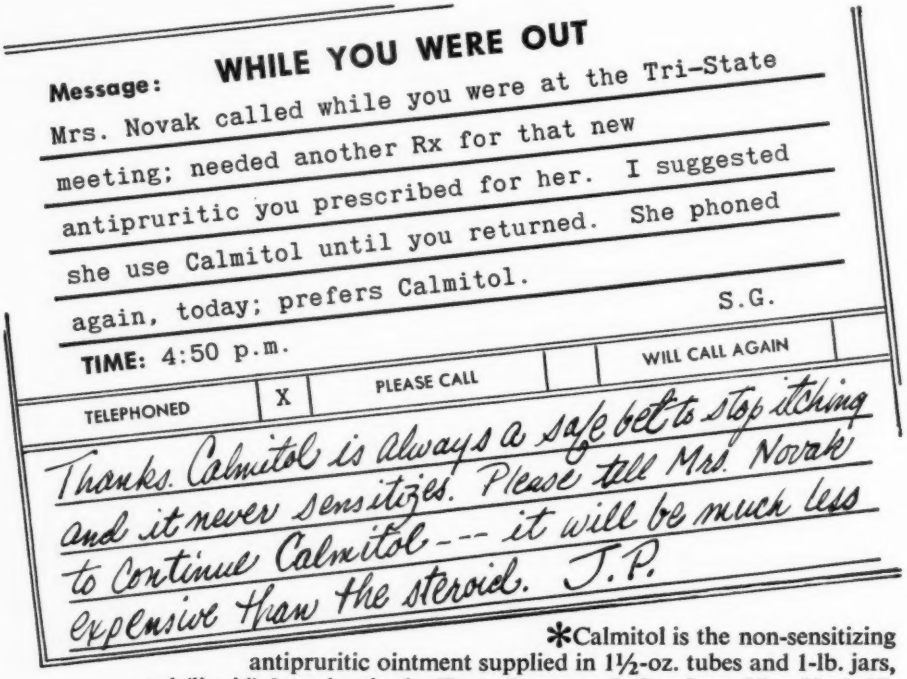
Petechial hemorrhages—Petechial hemorrhages in the brain, particularly in prize fighters, may be fatal shortly after trauma to the head. Most persons survive the effects of punctate hemorrhages, but complications develop later in life.

A young man, 20 years old, had participated in three rounds of boxing in an amateur contest. He dressed and rode home by public transportation. Arriving home, he complained of dizziness and headache and was lethargic. A physician was called, and he recognized some cerebral injury whose nature was not apparent and recommended hospitalization. The young man was dead on arrival at the hospital. Autopsy revealed punctate hemorrhages, many multiple, chiefly in the basal ganglia and cortical substance. The exact nature of the rupture of the small blood vessels was not ascertained, although one explanation proposed that a sudden change in the dynamics of the cerebrospinal fluid resulted from a blow or blows to the head, extending from the cortical area to the perivascular spaces in the brain.

Extradural hemorrhage—Hemorrhage into the epidural space results from injury to the middle meningeal artery, which is torn when the temporal bone is fractured. The accumulation of blood between the dura and bone exerts pressure on the underlying brain. The cerebrospinal fluid usually is free of blood and pigment, and when this condition is recognized clinically some relief can be provided by medical and surgical means without too serious damage.

Subdural hemorrhage—Subdural hemorrhage is usually venous and not arterial in origin, in contrast to extradural hemorrhage. It is one of the most common serious complications of blunt injuries to the head. Such an injury can cause symptoms or death weeks or months afterward.

(Continued on page A-70)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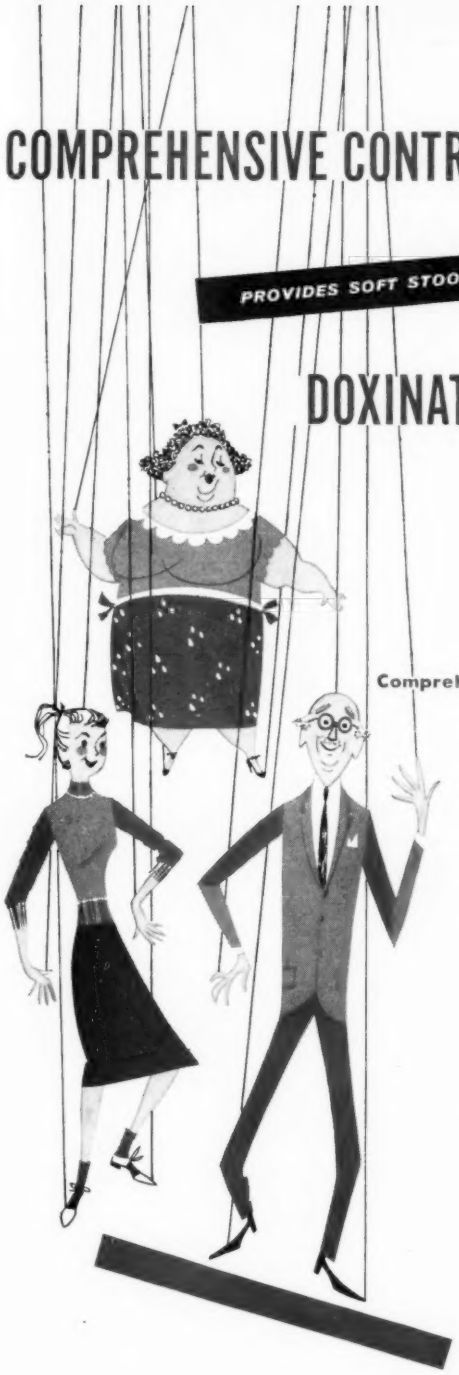

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It may be difficult to distinguish between non-traumatic and traumatic subdural hemorrhage. The hemorrhage is slow, and results from laceration of one or more thin-walled veins extending between the dura and arachnoid, although the force of the blow may be along the long axis of the skull. The injury may be minimal, such as a bump on the forehead or a fall out of bed, and the skull may not be fractured. Leary[2] observed that elderly persons, alcoholics and persons with severe arteriosclerosis are susceptible to subdural hemorrhage after relatively slight head injury.

Anatomic study demonstrates layers or areas of hemorrhage varying in color from red to green, suggesting more than one episode of hemorrhage beneath the dura. The hemorrhage may be localized or it may be diffuse over a large area. The greenish color obviously is due to the transformation of hematoidin to bile pigment.[3]

In subdural hemorrhage the cerebrospinal fluid may be xanthochromic, in contrast to the absence of pigment or blood in the spinal fluid in extradural hemorrhage. The interval following the appearance of subdural hemorrhage is important, because the blood clot does not absorb immediately. It is transformed into an area of liquefaction in which cysts may form later. At times I have found it difficult to state with certainty that a hemorrhage was entirely subdural, and I have observed hemorrhage between the layers of the dura mater which had perforated into the subdural space. The newly formed membrane may be made up of connective tissue and in some instances show the rich, vascular capillary bed.

Occasionally one sees subdural hematoma in inflammatory states involving the brain and in various blood dyscrasias. Differentiation from post-traumatic hematoma may be difficult. The following case illustrates this point.

A 45 year old white man had received injections of typhoid vaccine because of iritis. After the last injection he collapsed and fell, bruising his face and neck. He died shortly thereafter. Gross inspection of the brain revealed subdural local hemorrhages that could not be distinguished from traumatic hemorrhage except by microscopic examination. Moritz[4] stated that "it is frequently important in medicolegal cases to determine the pathogenesis of a subdural hematoma, and although in most instances the probable cause of the lesion can be recognized from its pathological characteristics, it is sometimes impossible to do so."

(Continued on page A-72)

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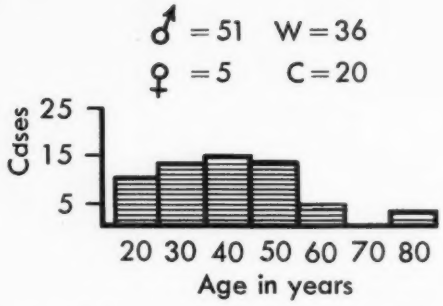

FIGURE 1. Bullet wounds with perforation and brain hemorrhage, 56 cases, referred immediately to coroner's office.

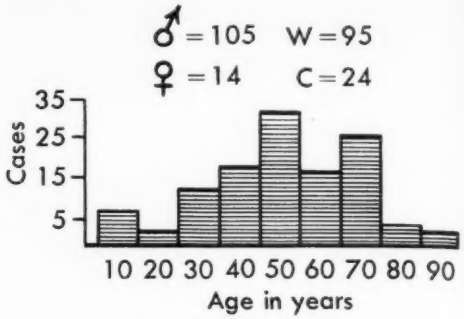

FIGURE 2. Skull fracture with brain laceration, 119 cases, referred immediately to coroner's office.

Subarachnoid hemorrhage—Hemorrhage into the subarachnoid space presents a problem because it may be either spontaneous or due to trauma. When trauma to the head has produced a penetrating and lacerating injury of the brain there will be evidence of subarachnoid hemorrhage, but not necessarily localized at the point of traumatic contact. Localization may be in other regions of the brain.[5] The presence of blood in the cerebrospinal fluid indicates subarachnoid hemorrhage but does not tell us whether it is of spontaneous or traumatic origin. Spontaneous subarachnoid hemorrhage may be preceded by headache, dizziness, stiffness of the neck, and varying degrees of coma, and in many cases the condition is diagnosed clinically as encephalitis lethargica.[6] In the early stages the spinal fluid may be xanthochromic, and later frank blood may appear. Spontaneous subarachnoid hemorrhage has many causes, including blows to the neck. When the autopsy surgeon sees this form of hemorrhage in the absence of a known and obvious penetrating or traumatic injury to the central nervous system, he has to be most circumspect in making a positive statement that the hemorrhage is traumatic or spontaneous.

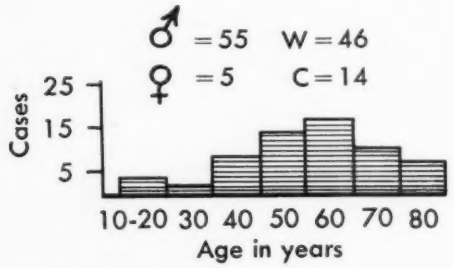

FIGURE 3. Skull fracture and complications, 60 cases. Many of these represent hospital patients, cases later referred to the coroner's office.

During the six year period covered in this study, all cases in which death followed traumatic injury to the skull and brain were referred to the coroner's office at the hospital. There were 56 cases in which a bullet had perforated the brain (figure 1). Some represented homicide, others suicide, and hemorrhage was extensive.

Skull fracture with laceration of the brain accounted for 119 cases (figure 2). Deaths in this group occurred mainly between the ages of 31 and 79 years. Males predominated, the ratio being 105 males to 14 females, and there were 95 white persons compared with 24 nonwhite persons. The skull fractures were produced by a fall or by some missile striking the head. In some cases the fracture penetrated the brain and in others there was a linear fracture with laceration of the brain and resulting hemorrhage.

We investigated 60 cases in which the patients had had fracture of the skull and complications had arisen (figure 3). The majority of these patients were between 41 and 79 years of age, and 55 were males. Forty-six were white and 14 were nonwhite. Death resulted from complications such as subarachnoid hemorrhage, abscess and epidural hemorrhage. Most of the patients did not die immediately. As a rule, death occurred several days after the skull fracture.

In persons of advanced age who have atherosclerosis, dizziness and unsteady gait, the tendency to fall or trip over objects is a hazard. A typical example of this group was the case of a

(Continued on page A-74)

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55 year old white man who left his home one evening to buy a package of cigarettes. A police officer found him lying on the sidewalk and could not arouse him. He assumed the man was drunk and put him in jail. After several hours the man's wife notified the police that her husband was missing and was told that he was found lying on the sidewalk, intoxicated, and was in the lockup. She objected strenuously, insisting that her husband never drank intoxicating beverages. Some time later he was found dead in the prison cell. Autopsy revealed a linear fracture of the right temporal bone with marked contrecoup hemorrhages in the brain. No alcohol or poisons were found in the organs, blood or urine.

Intracranial aneurysm—These aneurysms involve the arteries of the circle of Willis and the branches arising from it, and are nearly always extracerebral. They may be arteriosclerotic, mycotic or congenital in type.

Arteriosclerotic aneurysms occur in the older age groups. The vessels contain atheromatous plaques and invariably one finds evidence of atherosclerosis in the vessels in the chest and abdominal cavity.

Mycotic aneurysms usually result from an infective embolus originating in areas remote from the brain, such as from vegetations in bacterial endocarditis.

Congenital aneurysms of the circle of Willis are the most frequently encountered type. They are usually located in the middle cerebral, anterior cerebral and anterior communicating arteries, at the bifurcation of the arterial vessel wall. They are sometimes called berry aneurysms. The congenital aspect may be a thinning out of the middle coat of the blood vessel wall or the concentration of the elastic fibers in the internal elastic lamina. Atheromatous plaques may be deposited in the thinned-out wall, resulting in rupture of the aneurysm and hemorrhage in the subarachnoid space. If the aneurysm is situated on the anterior cerebral or anterior communicating artery between the frontal lobes, rupture may occur into the brain substance.

The question arises as to whether or not rupture of an aneurysm of the circle of Willis can follow trauma to the head. From the standpoint of criminal justice, an affirmative answer may lead to a charge of criminal assault. The anatomic location of a sacculated aneurysm involving the arteries in the circle of Willis is such that trauma, unless it is to the base of the skull with penetrating injury to the aneurysm, may result in rupture with extensive subarachnoid hemorrhage. However, these aneurysms usually are congenital and associated with a thinning and weakness of the muscular coat of the intracranial arteries. By examining the cerebral veins as they empty into the superior longitudinal sinus one finds it understandable that any injury, penetrating or closed, to the central nervous system may be associated with laceration or tearing of the cerebral veins, producing effusion and hemorrhage. Consequently, one sees hemorrhage involving the venous system more often than injuries involving the arterial system. The arteries in the region of the carotid foramen and within the cavernous sinus can be injured if a fracture involves the sella turcica. Thus the thin-walled arteries that make up the aneurysmal portion in the circle of Willis can respond more readily to stress without an external manifestation of trauma. A person who has an aneurysm of the circle of Willis may respond quickly to any factor, physical or psychic, that increases arterial blood pressure markedly.

The question is asked, Why did the aneurysm rupture at this time and not before under similar circumstances? One possibility is that with repeated stress and increase in blood pressure, particularly in hypertensive persons, the time comes when the dilated aneurysm no longer can withstand the continued intracranial arterial pressure. Finally it ruptures. The hemorrhage may be slight and the patient may recover, or it may be a severe rupture with massive hemorrhage.

Newbarr and Courville[7] stated that they believe physical injury to the head per se is rarely the primary cause of fatal rupture of congenital sacculated aneurysm. When fatal subarachnoid hemorrhage occurs during a fight, it is more likely that stress, with its attendant elevation of blood pressure, is the most important etiologic factor in rupture of the aneurysm, despite the blows to the head. It is important to bear in mind that trauma is not the all-important factor in rupture of aneurysm in the circle of Willis. Moritz[4] pointed out that "persons who have collapsed or died as a result of heart disease or apoplexy frequently come to the hospital or to the postmortem table with a diagnosis of cerebral injury."

Spontaneous Cerebral Hemorrhage

It may be difficult to demonstrate the pathologic changes in the vessel walls in cases of spon-

(Continued on page A-76)

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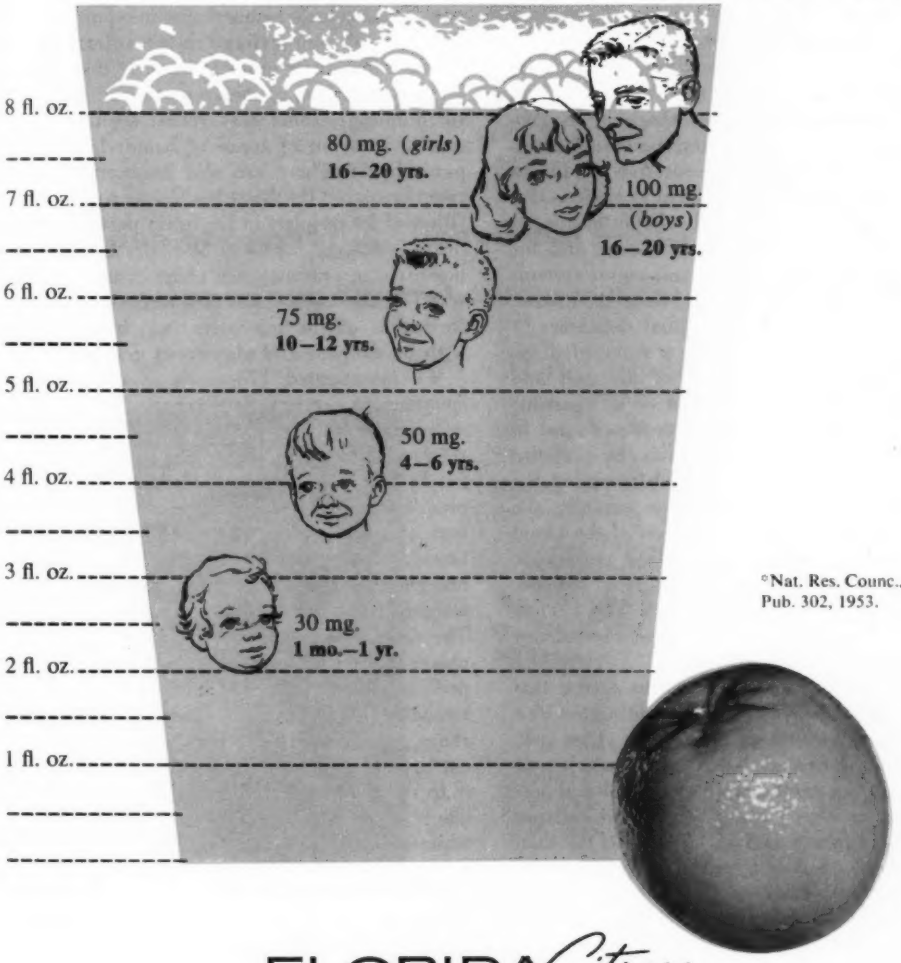

*Nat. Res. Counc., Pub. 302, 1953.

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taneous brain hemorrhage. Spontaneous punctate hemorrhages may occur in infections or toxic states and are rather common in association with poisoning from carbon monoxide or other agents. In poisoning from carbon monoxide the gross and histologic changes in the basal ganglia are fairly reliable diagnostic criteria. Histologic examination of these areas may reveal small zones of hemorrhage around blood vessels, and quite often the blood vessel walls themselves exhibit areas of necrosis with a zone of glial cells extending into the surrounding stroma. In toxic conditions due to noxious agents or carbon monoxide, it is postulated that the chemical produces necrotic areas in the small capillaries, injuring first the blood vessels, and that hemorrhage ensues later. Thus the hemorrhage is secondary to the degeneration of the blood vessels produced by the noxious agent, rather than vice versa.

Massive intracerebral hemorrhage—It is generally accepted that massive intracerebral hemorrhage is associated with degenerative conditions of the arterial vessels in the brain in various disease processes accompanied by hypertension or renal arterial disease. (Vascular tissue and the central nervous system are the two major systems that show the most devastating effects of disease, stress, overloading and nutritional deficiency.[8]) The patient's family will relate a story of dizziness; the patient lost control of his gait and either fell on the bathroom floor or bumped his head against an object, and later was found in a deep coma. The inclination is to pinpoint sudden coma to the injury which preceded the massive brain hemorrhage, when actually the necrotic and degenerative condition of the blood vessels, together with a generalized pathologic process such as cardiovascular or renal disease, provoked the massive hemorrhage. The hemorrhage was responsible for the patient's imbalance and caused him to fall.

The layman is most reluctant to accept this explanation. Some of our medical colleagues also argue against this sequence of events. They ask, Why, since the changes such as atherosclerosis were present the day before the accident and perhaps weeks or even months before, did collapse and coma occur now and not before? If the man had not fallen and bumped his head, massive hemorrhage in the central nervous system probably would not have occurred. Every physician has at some time encountered cases of hypertensive and cardiovascular-renal disease in which the patients died in their sleep without a history of trauma, and autopsy revealed massive intracranial hemorrhage. However, the fact remains that examination of the central nervous system in these cases shows extensive massive hemorrhage which may involve the lenticular nucleus and extend toward the surface of the brain and affect a large portion of the internal capsule. One may also see hemorrhage in the lateral ventricles of the brain. By careful dissection, if one can find the blood vessels in this area, one may demonstrate atherosclerotic plaques that are the only evidence of degenerative processes in the blood vessels before the onset of massive hemorrhage.

Generally, spontaneous pontine hemorrhage may rupture into the fourth ventricle. Spontaneous intracerebral hemorrhage may not present evidence of hemorrhage in the subarachnoid space, although it quite frequently does. Histologic examination of the area of hemorrhage and surrounding stroma may reveal edema and extensive invasion of zones of hemorrhage in the parenchyma. There are also degenerative processes involving the Nissl bodies, as well as deposition of fat droplets in the brain parenchyma. If death is delayed for 24 or 36 hours after massive hemorrhage one may see phagocytic cells filled with fat. These scavenger cells represent the transformation of the microglia, which are packed with fat droplets and pigmented granules.

We investigated 173 cases of death due to spontaneous cerebral hemorrhage, 100 of which represented hospital patients (figure 4), and 73 referred directly to the coroner's office (figure 5). In both groups the ages from 31 to 69 years predominated. The hospital group comprised 55 men and 45 women, and the ratio of white to nonwhite patients was 46 to 44. Blood pressure ranged from 120/80 to 240/150 mm. Hg. The weight of the hearts in this group is significant. The weight was from 300 to 745 gm. We have observed that a significant elevation of blood pressure and an enlarged heart indicate the potentiality of spontaneous intracerebral hemorrhage, which may follow in the wake of persistent hypertension.

In the group referred directly to the coroner's office there were 55 men and 18 women, 48 white and 25 nonwhite. We did not have blood pressure records for this group, but the heart weight was increased and there was generalized atherosclerosis as well as cerebral atherosclerosis.

Very little attention has been directed to the effects of violence or fatal injury to the head on

(Continued on page A-78)

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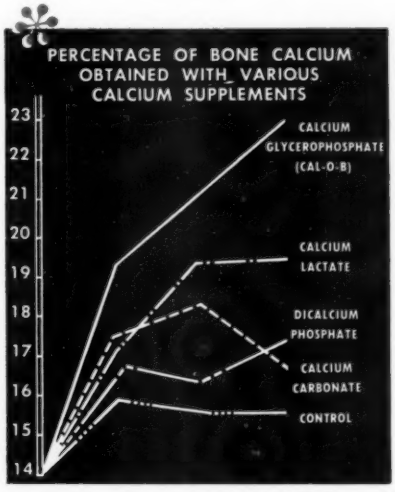

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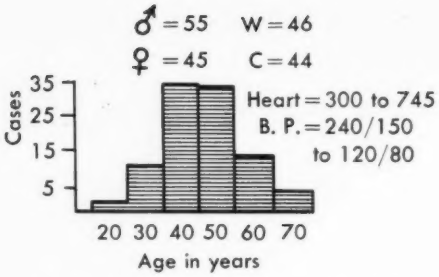

FIGURE 4. Spontaneous cerebral hemorrhage, 100 cases. Patients were admitted to the hospital and their cases were later referred to the coroner's office.

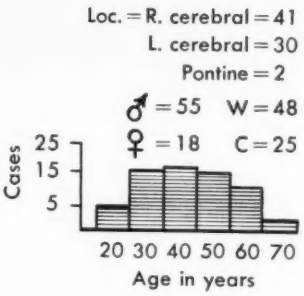

FIGURE 5. Spontaneous cerebral hemorrhage, 73 cases. Patients had a history of trauma and died before admission to the hospital.

the upper brain stem. Courville[9] discussed the effects of closed cranial injuries on the midbrain and upper pons in 284 fatal cases. He studied 33 cases in detail and summarized the effects as follows: (1) general, (2) pressure by local subdural or subarachnoid hemorrhage, (3) local injury, (4) coup-contrecoup mechanism, (5) lateral dislocation of the brain, (6) distortion of the midbrain, and (7) combined mechanisms. Courville expressed the belief that in 11 per cent of fatal cases of head injury there is some evidence at autopsy of injury to the upper brain stem—compression, distortion or hemorrhage in the segmental or basilar portion, or in both. Such lesions may be the result of traumatic shock to the head, air or fat embolism, local pressure by extramedullary hemorrhage, or penetrating injuries of the brain as from skull fractures or foreign bodies. Sudden lateral dislocations of the brain or a coup-contrecoup mechanism such as the sudden throwing back of the head, subdural accumulation of fluid, severe contusions, or hemorrhage with or without edema may produce similar pathologic alterations. Other factors too may predispose to their production, such as vascular anomalies or disease of the blood vessels in the brain. It is exceedingly difficult for pathologists to make an exact analysis and explain the underlying mechanisms when they encounter these findings.

Moritz[4] expressed the opinion that in about 25 per cent of all fatal craniocerebral injuries the skull escapes fracture. He pointed out that persons who have collapsed or died as a result of heart disease or apoplexy frequently have come to the hospital or the postmortem table with a diagnosis of cerebral injury. In reporting a study of age, change and adapted time in relation to aging and degenerative diseases, MacNider[10] said that the chemical basis for such alterations must develop years before structural changes appear. He stated: "Such retrogressive tissue modifications progress with periods of transitory tissue adjustment and with maladjustment until the latter state becomes permanent, fixed, and only stabilized as a state of disease or as physiological senility. Such states are not reversible, even though they may as such represent periods of tissue reaction in an attempt of stabilization." These changes become pronounced in the chronologic age development between 40 and 55 years. Thus when any accident is superimposed on pre-existing degenerative changes or when these alterations progress, life ends. What the pathologist observes is the end result of the continued pathologic-physiologic changes to the final stage of disease—namely, death of the cells. These observations are important. Pathology today is dynamic, and the pathologist along with his colleagues, particularly in the experimental areas, cooperate with the clinician in translating these tissue changes on preexisting clinical and altered physiologic states.

Cerebral Edema

For some time we have been conditioned to believe that cerebral edema is an important sequence in trauma of the central nervous system. There are varying and controversial opinions on this point. Some investigators believed that cerebral edema was the result of vasomotor disturbance following trauma (Scheinker and Evans[11]). Most forensic pathologists experienced in this field have been unable to corroborate this view. Many neuropathologists have attempted to cor-

(Continued on page A-80)

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1. Van Gasse, J. J., and Miller, R. F.: Current Concepts on the Etiology and Management of Atherosclerosis, Scientific Exhibit, American Medical Association Meeting, New York, June 3-5, 1957.

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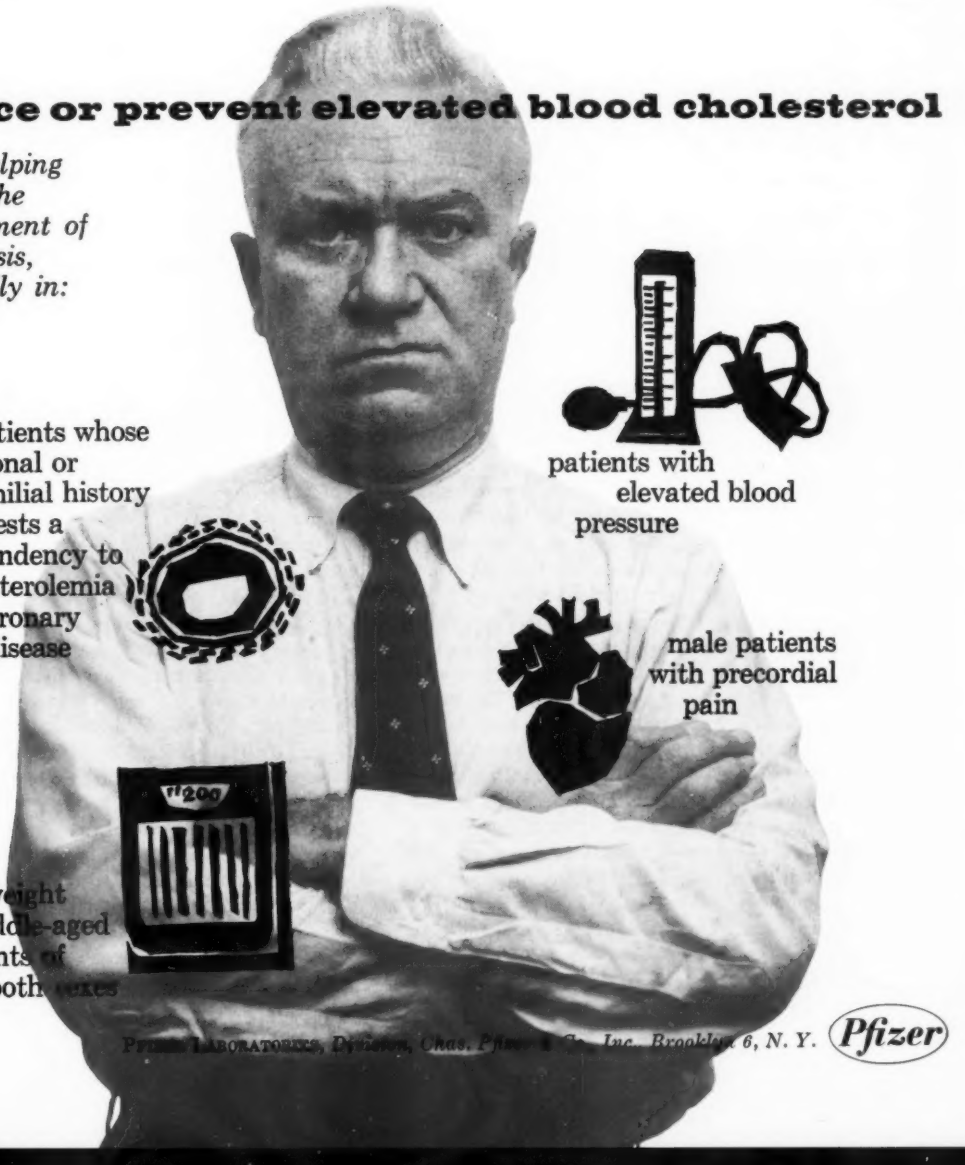

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TABLE 1

SPACE-DISPLACING LESIONS AND BRAIN TUMORS IN PATIENTS WITH HISTORY OF TRAUMA WHO DIED BEFORE ARRIVAL AT THE HOSPITAL

Brain abscess following scalp laceration (osteomyelitis)	4
Meningioma	3
Metastatic carcinoma	2
Meningo-endothelioma	2
Astrocytoma	2
Glioblastoma	2
Bulbar poliomyelitis	2
Cyst, pineal body	1
Cyst, cerebellum	1
Tuberculoma	1
	20

relate the accumulation of fluid in various nerve cells of the brain and the perivascular spaces as characteristic of head injuries. Pilcher[12] was unable to find any increase in fluid content of brain tissue in animals subjected to trauma sufficiently severe to increase the pressure of the cerebrospinal fluid markedly. One must remember that focal areas of edema may be seen in contusion and laceration of the brain and may follow any injury to the blood vessels. The important observation is that in severe and fatal injuries of the brain such as skull fracture with laceration of the brain and bullet wounds, edema usually does not occur.

Hassin[13] reported that accumulation of fluid in the parenchyma of the brain is not pathognomonic of head injury and is seen also in association with other nontraumatic pathologic processes in the brain. It may occur in hypertension, arteriosclerosis, and in cerebral insults from other causes, such as anoxia. One does not find in these brains the phenomenon of edema which some claim is the most typical feature of brain injury, and it has nothing to do with the changes in the blood vessels. The changes in the ganglion cells, nerve fibers and microglia are all produced by the injury, and one does not affect the other. It may be held by some that edema may be the only manifestation of brain injury and that all the changes that occur in the brain after injury are due to blood vessel alterations. This is subject to question. Quite often, when the cerebellar tonsils herniate into the foramen magnum, one is tempted to assume that this also is part of the alteration seen in cerebral edema. This is not necessarily true. There is no evidence of increase of interstitial fluid. If, following trauma to the head, the brain appears to be grossly larger than normal and there seems to be an excess of cerebrospinal fluid, this does not necessarily indicate edema of the brain. There may be ventricular dilatation, distention of the perivascular spaces (commonly seen in routine examinations of the brain), and foci of accumulated fluid in areas of tumor or abscess formation. These do not speak for edema but represent focal or perifocal zones of swelling. Courville,[14] as well as others, indicated that the accumulation of fluid, with resulting swelling of astrocytes, microglia and vascular endothelial cells, may contribute to cerebral swelling. Moritz[4] succinctly stated that "since there are, as yet, no generally accepted pathological criteria for the recognition of generalized cerebral edema, the problem must await further investigation before it can be regarded as settled." It is the consensus among forensic pathologists that cerebral edema is not an important diagnostic criterion in distinguishing between traumatic and nontraumatic processes of the brain, but that anoxia is unquestionably important as a factor in cerebral injury.

Neoplasms

Other pathologic processes of the brain are found at autopsy which give no hint of their existence during the life of the individual, but are discovered only after death following a head injury. In our study, 20 instances of miscellaneous neoplasms were found at autopsy (table 1). Again it is illustrated that a person may walk around with a brain tumor, undiagnosed clinically or misdiagnosed because psychiatric symptoms or behavior deviations mask the underlying lesion, and when he falls and injures his head the trauma is considered the causal factor in his death.

Huntington[15] reported his experience with primary intracranial neoplasms on a medicolegal autopsy service (as a hospital pathologist and coroner's physician in Bakersfield, California). During four years, 1000 coroner's autopsies were performed, including 275 hospital and coroner's cases and 911 routine hospital autopsies. In the latter group, eight cases of primary intracranial tumors were found, and in the coroner's series there were six intracranial neoplasms. The coroner's material suggested trauma, industrial poisoning, or postalcoholic or barbiturate withdrawal state. Thus it would seem that primary

(Continued on page A-82)

What is a Sensible Breakfast in Obesity?

IN the diet planned to reduce obesity it appears especially important that the total allowed calorie intake be well distributed over the day's customary three meals. A ratio of approximately 25% of the day's calories at breakfast, 35% at luncheon, and 40% at dinner has found wide acceptance.

Thus a sensible reducing regimen begins with a sensible breakfast—one which contributes a reasonable share of the day's total requirement of all essential nutrients, provides approximately one-fourth of the day's calories, and prevents undue hunger and helps maintain acuity during the morning hours.

A bowl of steaming oatmeal (¾ cup cooked oatmeal, 4 ounces skim milk, and 1 level teaspoon sugar) fits well into such a breakfast, whether the total calorie allowance be 1000, 1200, or 1600 calories per day.

Quaker Oats and Mother's Oats, the two brands of oatmeal offered by The Quaker Oats Company, are identical. Both brands are available in the Quick (cooks in one minute) and the Old-Fashioned varieties which are of equal nutrient value.

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Approximately 170 calories

Protein	9.0 Gm.	Folic acid	11.7 mcg.
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Thiamine	0.23 mg.	Phosphorus	235 mg.
Niacin	0.41 mg.	Potassium	325 mg.
Riboflavin	0.27 mg.	Zinc	1.53 mg.
Pyridoxine	0.13 mg.	Copper	0.35 mg.
Pantothenic acid	0.66 mg.	Manganese	1.45 mg.
Vitamin B_{12}	0.8 mcg.	Magnesium	65 mg.

A 300 calorie breakfast of 4 ounces of orange juice, the serving of oatmeal, a slice of lightly buttered toast, and coffee or tea (with artificial sweetener, if desired) is a sensible, satisfying, and nutritious morning meal in the reducing regimen.

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intracranial tumors may constitute an area of oncology with particular challenge for forensic pathology.

Bennett[16] reported on material from 84,615 cases received at the Army Institute of Pathology during World War II. The study was based on material collected from a selected age group, from 18 to 38 years. There were 446 intracranial tumors (0.5 per cent). Of these, 381 were classed as gliomas. The average age was 27.6 years. Of importance is the fact that 84 per cent of the patients had symptoms for less than six months, and those from 18 to 20 years of age did not have symptoms for longer than six weeks. Previous trauma was reported in 10 of 102 cases. Glioblastoma multiforme and astrocytoma were the next most frequently encountered tumors (22 and 14 per cent, respectively). Bennett compared his findings with a similar investigation made by Eldridge, Penfield and Cone[17] among civilians, and reported that gliomas occur in earlier decades of life.

Encephalomalacia

Encephalomalacia has various causes, but thrombosis and embolism are the chief etiologic factors. It has been calculated that as many as 1.8 million living Americans have had cerebral strokes at one time or another. Deaths from such strokes are estimated at 175,000 annually, and they are the nation's third ranking cause of mortality (*Science* 125:982, 1957). Interference with the blood supply to the brain leads to softening of the brain. Atherosclerosis of cerebral vessels with resulting anoxia of the brain may be reflected in the degenerative changes of the neurons and neuroglia cells with the end stage of gliosis. The appearance of small foci of cystic formation in the basal ganglia and cerebral cortex is not uncommon in persons of advanced years and in senile dementia. Many of these zones of softening may be overlooked in the fresh specimen, and the experienced pathologist will fix the brain; later, on sectioning, these areas are more pronounced. Histologic examination, especially with specific stains, will bring out the zones of softening more definitely.

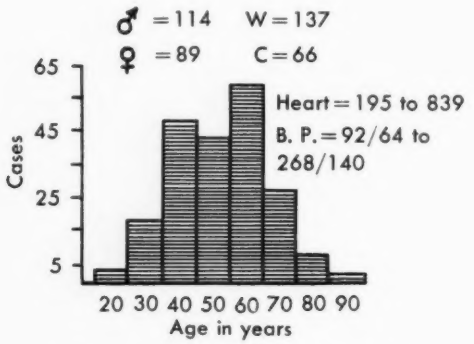

FIGURE 6. Encephalomalacia, 203 cases. Patients were admitted to the hospital with a history of trauma and their cases were later referred to the coroner's office.

Thrombosis is frequently associated with arteriosclerosis of the cerebral vessels, fibrosis of the pia-arachnoid, and atrophy of the cerebral cortex. In fact, these areas of softening may be in any portion of the brain—basal ganglia, internal capsule, cerebellum or brain stem. Embolism in the brain as a rule is not associated with arteriosclerosis and the underlying anatomic alterations cannot be readily distinguished from those due to thrombosis, except for the absence of fibrosis of the pia-arachnoid. The histologic appearance of these lesions is identical and independent of the nature of the occlusion: degeneration with infarction and softening and accumulation of gitter cells filled with fat and granules of blood pigment. The capillaries in the surrounding area are increased and prominent. Ultimately the degenerated area disintegrates and cysts form, surrounded by a layer of glia fibrils, and the cellular elements are swollen.

Figure 6 illustrates the age distribution of 203 patients admitted to the hospital with bizarre neurologic findings. After death, these cases were referred to the coroner's office for investigation because of a history of trauma prior to hospitalization or during the hospital stay. There were 114 men and 89 women, and 137 patients were white and 66 nonwhite. Note that there is a concentration of cases between the ages of 41 and 79 years. One would expect this in view of the pre-existing clinical pathologic states of hypertension and cardiovascular-renal disease. The minimal blood pressure was 92/64 mm. Hg. and the maximal 268/140 mm. Hg. The minimal weight of the heart was 195 gm., the maximal 839 gm. Thus the degree of rise in blood pressure and increased weight of the heart is not the only criterion to establish a correlation with softening of the brain, although the frequency of encephalomalacia may be more pronounced with a persistent increase in blood pressure. What is important is the atherosclerosis of the

(Continued on page A-84)

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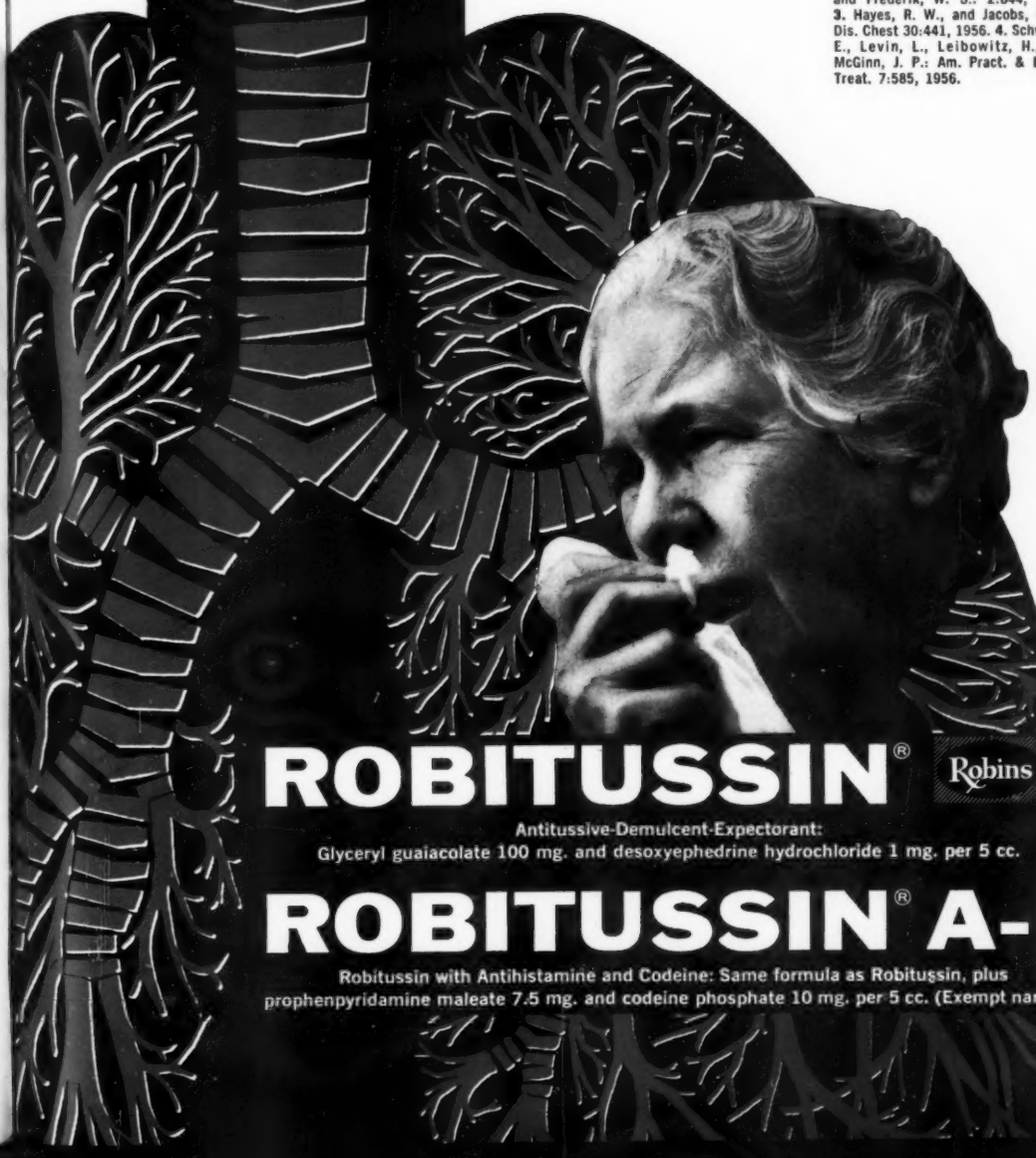

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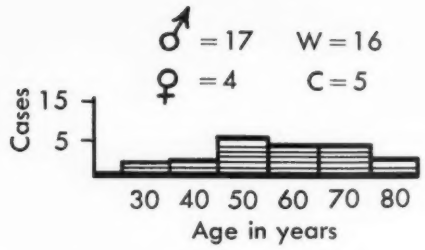

FIGURE 7. Arteriosclerotic encephalomalacia, 21 cases. Patients had history of trauma to the head.

cerebral vessels, which is usually associated with thrombosis.

In figure 7 are depicted 21 cases referred to the coroner's office with a history of trauma. The age group from 51 to 79 years predominated, simulating the group of 203 cases from the hospital (figure 6). There were more men than women (17 to 4) and more white patients than nonwhite (16 to 5). In this group, death occurred before referral to the coroner's office and hence we did not have records of blood pressure. The weight of the hearts was similar to that in the group of 203 hospital cases. The contusion, abrasion or laceration of the skin or scalp, in our judgment, was not related to the encephalomalacia, as these lesions were of longer duration and there was marked atherosclerosis of the cerebral vessels. The histologic alterations in the areas of softening were pronounced (Weil's stain).

According to the United States Bureau of Vital Statistics, in 1953 there were 826,890 deaths from heart disease, 242,430 from cancer, 91,270 from accidents, 25,000 from pneumonia, and 15,580 from tuberculosis. Bortz[8] stated that these figures indicate the underlying pathologic lesions which are the end result of these disorders and highlight the tissues of the blood vessels and nervous system as those showing the greatest destruction in our dynamic era.

Disorders of the vascular system cause some 770,000 deaths a year. Bortz reported that "men are about four times as susceptible as are women. Is this due to the unusual stress and strain to which men between the ages of 45 and 65 are subjected, or is there a basic superiority of the vascular tissues in women which gives them a greater stamina to withstand the insults of our current living?" It has been postulated that cholesterol deposits are seen more frequently in the coronary arteries of men than in those of women. If this is associated with underlying anatomic alterations supposedly inherent in the intima and media of the male vascular system, would this in part explain the greater incidence of cerebrovascular diseases among men than among women?

Summary and Conclusions

The frequency of spontaneous hemorrhage of the brain and encephalomalacia among cases referred from the hospital with a history of trauma such as contusion and laceration of the face and scalp, or alleged trauma, is compared with a group of cases with similar histories and pathologic findings referred directly to the coroner's office for investigation. The study covered a period of six years.

There were cases of skull fracture with penetration of the brain, bullet wounds, and "closed" injuries of the brain. In 20 cases with histories of head trauma, autopsy revealed various space-displacing lesions and neoplasms.

Edema of the brain is not pathognomonic of traumatic injury of the brain. Cerebral edema is seen in various toxic and noxious processes of the brain including spontaneous subarachnoid hemorrhage and abscess.

In the United States there are approximately 43,000 accidental deaths and 1.5 million injuries per year. It is appalling that death from accidental injury during peacetime exceeds the death rate from modern catastrophic war. A large number of casualties occur from industrial hazards in our present age of technocracy. In evaluation of cause and effect, one is confronted with the question, Is the injury responsible for the death or are the anatomic findings independent of injury? The hospital pathologist and coroner's autopsy surgeon have a grave responsibility in these matters.

The entire personnel of the coroner's or medical examiner's office serve the community, and their objective is to aid the law-enforcing bodies in establishing civil and criminal justice. The pathologist's role is an important one, and his findings and interpretation may mean the difference between life and death or liberty and imprisonment, or may mean financial responsibility to an individual or organization.

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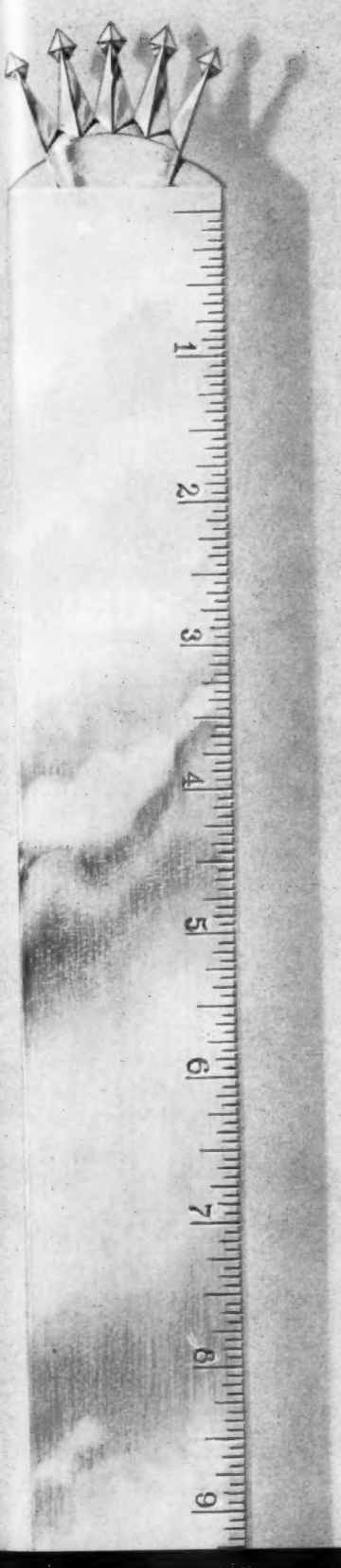

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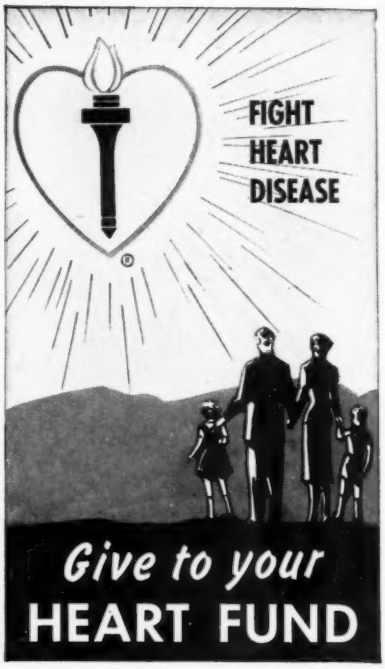

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Postgraduate Medicine

FEBRUARY 1958

SPECIAL ISSUE

University of Colorado School of Medicine

DENVER

ROBERT J. GLASER, M.D.
Guest Editor

INTRODUCTION

THE faculty of the University of Colorado School of Medicine is pleased and privileged to participate in this special issue of POSTGRADUATE MEDICINE. The contributions of the various authors, which represent a few of the many areas of interest of our faculty, were selected in the hope that they will prove stimulating to the readers of this journal.

With the view that a résumé of the history of this school would be of interest, the following brief summary is presented. The University of Colorado Medical Department was initiated in 1883 at Boulder, the site then and now of the University of Colorado. In 1892, the medical department was moved to Denver, but this move, contested by the medical faculty of Denver University, was ruled unconstitutional by the state supreme court, and the program was perforce returned to Boulder.

In 1887, the Gross Medical College was chartered as the Medical Department of Rocky Mountain University, the only active unit of this institution. It grew in strength and eventually, in 1902, merged with the medical department of the University of Denver.

Repeated attempts by the University of Colorado to gain legislative permission for the medical department to establish itself in Denver once more were partially successful in 1909, when approval was given for the teaching of the last two years in Denver. In 1911, shortly after publication of the famous Flexner report, the Denver and Gross College of Medicine combined with the medical department of the University of Colorado School of Medicine, which then had its modern beginning.

Initially, the courses of the first two years were taught in Boulder, and the last two in Denver. The clinical faculty was steadily improved in caliber; notable strength was derived from the addition of men such as Henry Sewall, who came to Colorado for reasons of health.

In 1922, a constitutional amendment was passed permitting transfer of the entire medical teaching program to Denver; in 1924, the present buildings, made possible to a significant degree by the generosity of Denver citizens and of the General Education Board of the Rockefeller Foundation, were occupied.

The past 33 years have seen remarkable growth, not only in the student body, which has increased from 50 to 85 members per class, but also in the size and caliber of the faculty. All departments are now headed by full-time men, and include a full-time nucleus. The important contributions of a large and able volunteer faculty, working with the full-time group, have made possible a well-rounded teaching program for medical students, residents and fellows. In addition, the medical school faculty has an important role as a division of the Graduate School of the University of Colorado.

We now look forward to a building program which promises new facilities for both basic science and clinical departments. The planned additions will provide much needed space for the extensive programs now in operation, and will make possible a continuation of the development which has characterized the University of Colorado School of Medicine.

ROBERT J. GLASER, M.D.
Dean and Professor of Medicine
GUEST EDITOR

Preinvasive Cancer of the Uterine Cervix

E. STEWART TAYLOR AND LOUISE C. WALKER*

University of Colorado School of Medicine, Denver

THIS is a report of our experience with preinvasive cancer of the cervix over the past nine years at the University of Colorado. It is difficult to be certain that a particular lesion is preinvasive cancer rather than squamous metaplasia, atypical hyperplasia or glandular replacement, and we undertook this study to determine if the diagnosis of preinvasive cervical cancer was being made too often and if the treatment was too radical.

Preinvasive cancer of the cervix is the subject of much discussion in every hospital and clinic because of the frequency with which the diagnosis is considered. Papanicolaou and Traut[1] placed vaginal cytologic screening methods on a firm base with their monograph in 1943. In the subsequent 15 years, wide application of this procedure has led to the diagnosis of countless early and preinvasive cervical cancers. Papanicolaou's work dates back to 1917 when he and Stockard[2] reported a morphologic study of the sequence of cyclic changes in the reproductive organs of female guinea pigs. In 1923 he transferred his effort to a study of the menstrual cycle in women.[3,4] It was then that he made his chance observations on cancer cells found in vaginal secretions: "The first observation of cancer cells in a smear of the uterine cervix was one of the most thrilling experiences of my scientific career. The striking morphologic characteristics of cancer cells and of their nuclei could not possibly fail to impress anyone seeing them for the first time."[4] Twenty years and several publications later these chance observations of Papanicolaou were finally accepted as impor-

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tant, practical, reliable and helpful in the detection of early cancer.

Were it not for the practical value of the Papanicolaou vaginal cytologic test, few preinvasive cervical cancers would be found. We feel we are diagnosing early cancer in increasing numbers, but we must be including some benign lesions such as atypical epithelial hyperplasia, cervical metaplasia and glandular replacement of the cervix.

The concept of superficial or preinvasive cancer of the cervix was proposed as early as 1910 by Rubin[5] and in 1912 by Schottlaender and Kermanner.[6] Schiller[7] in 1933 gave impetus to the concept. TeLinde and Galvin[8] deserve the most credit for popularizing the idea of carcinoma in situ by calling it to our attention and aiding in delineating the histologic criteria. They published their first paper on the subject in 1944, and even now, 14 years later, experienced pathologists do not agree completely about preinvasive carcinoma of the cervix.

The number of patients with preinvasive cancer of the cervix who have been followed in various clinics is large enough so that we know that if left to its own course the lesion will progress in 6 to 10 years to invasive cancer. Now, however, we are uncertain whether or not all lesions labeled carcinoma in situ of the cervix are true preinvasive cancers.

Material and Method

The Papanicolaou vaginal cytologic test has been a routine screening procedure in our clinic since December 1947. Between December 1, 1947, and January 1, 1957, we detected 51 cases of preinvasive carcinoma of the cervix. Another 20 patients came under our care in whom the diagnosis had been made by primary biopsy. During this nine year period we tested 11,342 patients by means of the vaginal cytologic procedure in our clinic. This number included all new gynecologic patients over the entire period and all prenatal patients seen during the past six years. Other positive and suspicious Papanicolaou tests were encountered, but 51 of the 11,342 patients screened were finally diagnosed and recorded as having carcinoma in situ of the cervix.

After a positive Papanicolaou test report is received, a cold-knife cone biopsy is done in the hospital operating room. The three stage uterine biopsy is taken (1) from the squamocolumnar junction of the cervix, (2) from the endocervix, and (3) from the endometrium. Tissue removed by punch biopsy often is insufficient for an accurate diagnosis. The cone biopsy specimen is taken to substantiate or rule out a diagnosis of preinvasive carcinoma or, possibly, invasive carcinoma.

The patients in our series of cases of carcinoma in situ of the cervix ranged in age from 21 to 70 years. The fourth decade of life accounted for the largest group, rather than the fifth decade, which predominates in cases of invasive cervical cancer. The age distribution in our series is to be expected, since it takes 6 to 10 years for preinvasive cancer to become invasive.

All the patients except one were married, and all but five had had children. The one unmarried patient had been pregnant. This finding is in keeping with the fact that cervical cancer is a disease of the noncelibate.

The presenting complaints in these cases are interesting in that there were relatively few of the classic symptoms usually attributed to early cervical cancer. Approximately one-third of the patients were seen because of pregnancy. One-third had a menstrual disorder or vaginal discharge, and the remaining third had various complaints, none of which suggested early cancer. This emphasizes that carcinoma in situ is a disease without signs or symptoms and therefore can usually be discovered only by Papanicolaou vaginal cytologic testing followed by adequate cervical biopsy.

Treatment

Fifty-three of the 71 patients received definitive treatment at our institution. Fifty had hysterectomy (either vaginal or abdominal), three received radium treatment, and 18 had only a cervical conization. The radium treatment was given because the general condition of the patients contraindicated major surgical treatment.

The hysterectomy in each instance was a total abdominal or vaginal one, and care was

taken to extend the operation sufficiently to remove 2 cm. of the upper vagina. The tubes and ovaries were not removed, nor were parametrial tissues or lymph nodes. There were no operative deaths, and cancer has not recurred in any case after treatment.

Discussion

Experienced pathologists and gynecologists will agree that uncertainty surrounds the microscopic diagnosis of carcinoma in situ of the cervix in approximately half the cases in which the diagnosis is considered. This is the main problem with the lesion. It is necessary to study each patient individually and elect treatment only after adequate histologic study of sufficient biopsy material. One must consider the patient's age, marital status, and future childbearing career, along with the biopsy evidence, before advising treatment.

Is hysterectomy too much or too little treatment for a carefully diagnosed cervical carcinoma in situ? In 17 of our cases neoplastic tissue could not be found in the operative specimen after hysterectomy. One must assume, therefore, that in these instances adequate conization of the cervix removed all evidence of cancer and that hysterectomy was not necessary. Against this we must balance the surprise finding of early invasive lesions in three of the operative specimens, lesions previously judged as preinvasive. The invasive lesions were unsuspected and theoretically undertreated. The three patients, however, seem to be cured in spite of oversimplified treatment. None of them have had postoperative deep x-ray or radium treatment.

In 18 cases we elected to follow the patients conservatively for reasons of their youth and their desire to have more children. Only cone biopsy was performed in these cases. Four patients have been lost to our follow-up, and one died of adenocarcinoma of the rectum. Cone biopsy and repeated Papanicolaou tests have been performed in the remaining 13 cases, and 11 of the patients are free of any biopsy or vaginal cytologic evidence of disease.

In 20 of the 71 cases of carcinoma in situ the lesion was detected during pregnancy or after an abortion. When the diagnosis was made during pregnancy, no treatment was given. Further cytologic tests and cone biopsies were done four months after delivery, when involution was complete and the pregnancy changes in cervical squamous tissue, which may be indistinguishable from superficial cancer, had receded. In five of the 20 cases the changes thought to have been carcinoma in situ had disappeared spontaneously.

According to Randall and Gerhardt,[9] cancer of the cervix may be expected to develop in 2 per cent of all women more than 40 years of age. The incidence of recognizable cervical cancer among patients over the age of 30 years examined in a cancer detection clinic during five and one-half years was one in 625 patients.[10] In a nine year study we have made a diagnosis of preinvasive cancer in four of each 1000 vaginal cytologic examinations. This is more frequent than cancer should be statistically anticipated.

Summary

Our experience at the University of Colorado with carcinoma in situ of the cervix is reviewed and analyzed. In a nine year period 71 patients were diagnosed as having preinvasive carcinoma. The larger share of diagnoses may be credited to information gained by cytologic screening procedures. The methods of diagnosis and management are reviewed. Calculations on the expected incidence of cervical cancer are made with a view toward determining if the diagnosis of cancer in situ has been made too often.

Conclusions

1. The Papanicolaou vaginal cytologic test has been most helpful in detecting preinvasive cancer of the cervix.

2. Excision cone biopsy is desirable to confirm the diagnosis of preinvasive cancer and to rule out invasive cancer.

3. Total abdominal or vaginal hysterectomy with excision of 2 cm. of upper vagina is the preferred treatment.

4. Pregnant patients and young patients who have not had their families should be treated conservatively and followed.

5. It is apparent that even with careful se-

lection we have made the diagnosis of carcinoma in situ more often than one would expect in this number of patients.

6. A patient in whom a diagnosis of carcinoma in situ of the cervix is made in our institution has a 44 per cent chance of cure by simple cone biopsy alone.

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Postgraduate Clinical NOTES

87. VAGINAL CYTOLOGY

In the United States vaginal cytology is far more widely practised than in this country, and routine visits for a vaginal smear are encouraged by many gynaecologists. In this country its employment has been limited to screening patients attending outpatient clinics, and so the clinical material is already partly selected and the figures quoted do not give as true a picture of the numbers of cases of unsuspected carcinoma that could be diagnosed by cytology in the population at large. The difficulties in establishing cytology as a routine in all gynaecological clinics are essentially practical ones. There is at present a limited number of trained technicians available, and because the work is essentially tedious, time-consuming and limited by such factors as eye fatigue, it would be difficult to recruit a sufficient number to do the work apart from the economic factors involved. In an average outpatient department it might well require six months' work by a technician to pick up a single positive smear. Among the experts there is still no unanimity of opinion about the treatment of carcinoma *in situ* once diagnosed. We know that about one-quarter of the cases diagnosed progress to invasive cancer within 10 years, but we do not know the natural history of the condition and whether in those cases in which spontaneous regression occurs it is permanent or liable to recur at a future date, or whether all invasive cancers pass through a phase of an *in situ* lesion. Within the foreseeable future in this country it seems that vaginal cytology must be limited to a few centres where research and detailed follow-up of individual patients may be made.

J. H. Peel, Advances in obstetrics and gynaecology, *Practitioner*, October 1957, p. 375

Acute Ataxia of Childhood

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THE purpose of this paper is to call attention to the serious problem of ataxia of acute onset in childhood. I shall describe a previously unreported case and discuss certain aspects of the syndrome. Although the entity has been recognized for some time, there are only sporadic references to it in the literature[1-5] and standard pediatric textbooks offer little or no discussion of it. The syndrome is usually referred to as acute cerebellar ataxia, but there is meager conclusive evidence that it is cerebellar in origin.

Report of Case

A three and one-half year old white girl was admitted to Colorado General Hospital on December 13, 1956. The chief complaints were staggering gait, loss of equilibrium, and tremulousness. She had been well until 11 days before admission, when it was noted that her knees trembled when she walked or stood. Unsteadiness of gait continued, and three days later she became irritable and complained of nausea. Four days before admission she could no longer feed herself because of incoordination of the arms, and a marked tremor of the entire body developed when she tried to sit. Her speech became slurred and she began to have difficulty in handling pharyngeal secretions. The day before admission it was noted that her eyes danced when she tried to fix her gaze to either side, and she vomited after meals.

History—Review of her past history did not disclose any unusual findings in regard to her birth, the neonatal period, or development. Routine immunizations had been done in infancy, and she had received two doses of poliomyelitis vaccine four months prior to the present illness. Eight months before she was admitted to the hospital she had had mumps, but there had not been any recent illness or known exposure to contagious diseases. The systemic review and family history were not unusual.

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Physical examination—Blood pressure was 100/80, pulse 80, and temperature 37° C. Respirations numbered 22 per minute. Positive findings were limited to the neurologic examination. The patient was well developed and well nourished and appeared somewhat apathetic and lethargic. She responded to questioning intelligibly but in a disinterested fashion.

The pupils were round and equal and responded to light and accommodation. Extraocular movements were executed with a marked nystagmus on right, left and upward gaze. Examination of the fundi showed normal maculae and peripheral retinas. The disks were of normal color, the vessels were not engorged, and the margins were sharply demarcated. Physiologic cupping of the disks was evident. There was no papilledema. Hearing, taste and smell were normal.

No abnormalities of the cranial nerves were elicited. Examination of the neuromuscular system did not reveal wasting or abnormal movements of the trunk or extremities at rest. With passive movement of the extremities the tone was profoundly decreased bilaterally and symmetrically. Muscular strength was difficult to evaluate but seemed generally decreased. When the patient attempted the finger-nose test there was a marked tremor of the hand throughout the entire range of movement. Marked incoordination was similarly evident when the heel-knee test was performed. When an attempt was made to have her sit, a severe tremor of the trunk developed, causing her to lose her balance and fall backward.

There were no abnormalities of sensation. The jaw reflex was not elicited. Deep tendon reflexes of the upper extremities were barely perceptible and were symmetrical. Abdominal reflexes were equal and normal. Ankle reflexes and knee jerk reflexes were hypoactive bilaterally. Attempts to elicit the plantar reflex produced a flexor reaction.

The patient had a slurring dysarthria of such severity that her speech was difficult to understand. She was unable to stand without support, and attempts to walk with support produced severe ataxia of both the trunk and extremities.

Laboratory and roentgenologic findings—Hemoglobin was 15 gm. White blood cell count was 7,750 (neutrophils 53 per cent, lymphocytes 43 per cent, monocytes 3 per cent, eosinophils 1 per cent). Urine was normal. Culture of material collected from the throat showed occasional pneumococci, alpha hemolytic streptococci and *Neisseria catarrhalis*. A tuberculin test was negative.

Roentgenograms of the skull taken on admission did not show signs of increased intracranial pressure or other abnormalities. An electroencephalogram was normal.

Hospital course—The child was observed closely for four days. During this period there was no change in symptomatology. She remained afebrile, vomited occasionally, and continued to have body tremor and ataxia on attempted movement. The optic fundi remained normal. Because she failed to improve during this period of observation, ventriculography and pneumoencephalography were performed on December 18. Abnormalities of the ventricular system were not demonstrated. The cerebrospinal fluid did not contain cells, the amounts of protein and sugar were normal, and culture of the fluid was sterile.

Following these studies, the patient's condition changed little. Marked ataxia persisted and she continued to vomit occasionally. Sixteen days after admission she was dismissed from the hospital to be followed as an outpatient. Her condition was the same as it had been on admission.

Subsequent course—Within a few days after dismissal from the hospital the patient began to improve slowly and progressively. The body tremor subsided and she began to sit alone without support. Shortly thereafter she could feed herself, and within two weeks she was trying to walk alone. Nystagmus persisted for approximately six weeks. Two months after the onset of the symptoms she could walk, run and perform fine movements with minimal disability. When she was seen after six months the only positive finding was a minimal unsteadiness when she turned about quickly. Otherwise the recovery has been complete. Heterophilic agglutinins and agglutinins for neurotropic diseases were not demonstrated.

To summarize this case report, a three and one-half year old girl experienced the sudden onset of ataxia, dysarthria, nystagmus and truncal tremor. Results of routine laboratory procedures were within normal limits. Ventriculography and pneumoencephalography did not reveal deformity of the ventricular system. The patient's condition remained stationary for three weeks, after which the symptoms and signs cleared spontaneously over a one month period. Cultures and serologic study did not reveal a specific etiologic agent.

Discussion

This case has been reported in considerable detail as it seems to be fairly typical of those reported previously. Several diagnostic possibilities were entertained initially. Among them were midline medulloblastoma, hemangioblastoma and astrocytoma of the roof of the fourth ventricle. They were considered unlikely in view of the sudden appearance of incoordination of such a marked degree. Tumors in this area usually produce symptoms of a more insidious onset. A tuberculoma of the midline cerebellar structures seemed improbable in view of the negative tuberculin test. The absence of an antecedent infection and of localization to one cerebellar lobe, and the normal temperature and peripheral blood picture seemed to rule out a cerebellar abscess. Tumors of the pontine or midbrain region seemed doubtful in the absence of long-tract signs or abnormalities of the cranial nerves. The family history and the acute onset of symptoms were not compatible with a progressive degenerative disease. There was no history or evidence of an ear infection to suggest acute labyrinthitis. Indeed, all we could determine definitely was that the patient had acute ataxia of unknown etiology.

Investigation of the ventricular system from above was undertaken to rule out a space-occupying lesion. Only after a normal ventricular pattern had been demonstrated did we feel secure in entering the subarachnoid space. Had a space-occupying lesion been present in the posterior fossa or above it, the removal of cerebrospinal fluid conceivably could have produced herniation of the cerebellar tonsils and brain stem through the foramen magnum. After completion of the air studies it was felt that further investigation was not indicated and that the child should be watched closely. The subsequent course proved most gratifying.

Groups of cases representing the syndrome of acute ataxia of childhood have been reported by Klingman and Hodges,[1] Shanks,[2] Berglund, Mossberg and Rydenstam,[3] and Cottom.[4] The pattern of the case reported herein is quite typical of their cases. The syndrome has occurred after measles, mumps, varicella and influenza, but in more than 70 per cent of the cases there has not been an antecedent infection. When an infection has preceded the ataxia, an interval of three to seven days has elapsed between the infection and the appearance of ataxia.

The striking feature of the syndrome is the rapid development of ataxia over a period of a few hours followed by a stationary status varying in duration from two weeks to two months. Dysarthria and ataxia characterize the clinical picture. Nystagmus is an inconstant feature. Tremors of the trunk were described in several of the reported cases. Myoclonic seizures and choreiform movements also have been noted. Examination of the cerebrospinal fluid has revealed quite variable cell counts ranging from no cells to 30 to 50 lymphocytes. The amounts of protein and sugar in the cerebrospinal fluid have been within normal limits on initial examination, but subsequently, in the convalescent period, the protein has been reported to be quite elevated. Berglund and associates[3] described transitory electroencephalographic changes.

As already mentioned, there is no pathologic evidence to incriminate the cerebellum as the exclusive site of origin of this syndrome, and the cerebellar symptoms might be only a part of a diffuse encephalitic process. Klingman and Hodges[1] pointed out that the symptomatology could result from lesions of the red nucleus, the brachium cerebri or the labyrinth. Furthermore, it is not unusual to see acute ataxia develop during a patient's recovery from acute encephalitic processes. Such a sequence is well known following measles, and

it has been described in detail by Ford.[5]

The etiology of such cases remains obscure. The work of Berglund and associates[3] suggests that in some instances poliomyelitis might be the causative agent. Cottom[4] reported isolating a virus, as yet unidentified, in one case. We recently observed the development of acute ataxia following an infection which was believed to be caused by influenza A, as a sharply rising titer of antibodies against this virus was demonstrated.

The prognosis of acute ataxia is generally favorable. The ataxia decreases within two weeks to two months, and rapid improvement usually ensues. Minimal residua may persist for long periods. When there is evidence of a more diffuse involvement of the central nervous system, prognosis should be guarded. The series of cases reported by Klingman and Hodges[1] included one in which the patient was later institutionalized because of severe behavioral disturbance.

Summary

Attention is called to the syndrome of acute ataxia in childhood of unknown etiology. It is characterized by dysarthria and incoordination suggestive of cerebellar ataxia. Nystagmus is often a feature. A case is reported in detail, and various aspects of the entity are discussed.

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Postgraduate Clinical NOTES

88. PAIN

The development of pain clinics seems to be inevitable, as cases of chronic pain require special study, both from the physical point of view and from the need to assess and adjust any abnormal mental attitude to the symptoms. Even when the psychological factor is very prominent the best approach is often a purely physical one, provided that one remains conscious of the need to do everything also to readjust the mental attitude. Not so long ago it was generally thought that to relieve chronic pain it is necessary to divide or otherwise destroy nerves going to the painful part. This attitude, however, is being revised as it has become clear that the central thresholds may remain very low after nerve section. Thus, in post-herpetic neuralgia the most successful treatment is directed to the scarred area of skin, especially to hyperaesthetic zones where vigorous massage, exercises, local lignocaine and electrical massagers give relief to the most stubborn cases. Rest with protection to the scarred area is the worst thing to advise.

W. Ritchie Russell, Advances in neurology, *Practitioner*, October 1957, p. 419

Colorado Tick Fever

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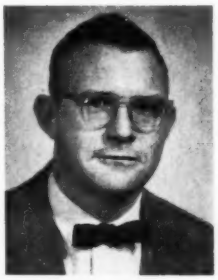
COLORADO tick fever has a specific regional and seasonal incidence and a characteristic clinical pattern. The disease is caused by a virus transmitted to man by the adult hard-shelled wood tick *Dermacentor andersoni*. The incubation period is usually four or five days. The illness occurs throughout the Rocky Mountain region from early spring to early autumn, with the peak incidence from April through the middle of July.

The clinical picture is characterized by a fairly abrupt onset with chilliness, fever, malaise, retro-orbital pain, backache and muscle ache. There is no rash and the physical findings are not specific. The spleen may be palpable. Generally the illness is phasic with two febrile periods of two or three days separated by a one to two day remission. Occasionally there are three or more exacerbations; rarely there is only one. Moderate to marked leukopenia is a consistent feature. The outcome is almost always favorable, although convalescence may be prolonged. Meningitic and encephalitic complications have been described recently.[1,2]



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GORDON MEIKLEJOHN

Diagnosis can be made on clinical grounds with a high degree of accuracy and confirmed in the laboratory by isolation of the virus from acute-phase serum and by demonstration of specific neutralizing and complement-fixing antibodies.

Background

Curiously, in spite of its rather consistent clinical course and distinctive epidemiologic pattern, Colorado tick fever was not recog-

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nized as a specific disease entity until the twentieth century. During the late nineteenth century, clinicians of the Rocky Mountain region noticed that certain cases of "mountain fever" were benign and easily treated, but the syndrome was generally accepted as a form of typhoid, malarial or enteric fever.[3-6] The seasonal incidence and the descriptions of patients[3,4] correspond to current information concerning Colorado tick fever, leaving no doubt of its presence in the Rocky Mountain area long before its identification. Nevertheless there was no more than suspicion that a disease similar to Colorado tick fever should be separated from other mountain fevers until 1907 when Kieffer,[7] a military surgeon who had been stationed at Fort D. A. Russell, Wyoming, published the first definitive account of a remittent, nonexanthematous tick-borne fever in the Rocky Mountain area. His patients had three or more febrile periods and did not have leukopenia, and a significant anemia developed which suggested hemolysis. Otherwise the illness was similar to the usual case of Colorado tick fever.

During the 1920s, Becker[8,9] of Denver investigated the prevalence and distribution of Rocky Mountain spotted fever and other illnesses transmitted by the wood tick. On clinical grounds he clearly separated Colorado tick fever as a distinct entity. In 1930 and 1931, Toomey[10,11] reviewed extensively the regional literature on tick-borne diseases, especially Colorado tick fever, which he called American mountain tick fever. He emphasized the clinical pattern and discussed the various modifications of the usual biphasic course. The leukopenia which regularly accompanies the acute illness was first reported by Topping, Cullyford and Davis[12] in their careful study of Colorado tick fever in the Boulder, Colorado, area in the spring of 1940.

In 1944, Florio, Stewart and Mugrage[13] of the University of Colorado produced the disease in human volunteers by inoculation of blood from persons who had Colorado tick fever. They further demonstrated that the virus could be propagated in hamsters, in which it produced marked leukopenia. Later, Florio and associates[14] showed that the virus could be obtained from *Dermacentor andersoni* collected in areas known to be endemic for the disease. Subsequently the virus was successfully adapted to mice and developing chick embryo.[15] Virus can be obtained from blood drawn during the acute illness, including the afebrile remission.[16] Florio and associates[17] reported that virus also can be obtained from spinal fluid during the phase of viremia.

In the past 10 years the epidemiologic pattern of Colorado tick fever and its clinical and immunologic aspects have been studied extensively. According to current knowledge the disease is truly regional, no case having been contracted outside the Rocky Mountain area. Cases have occurred in nearly every Rocky Mountain state. Eklund and co-workers[1] have isolated virus from the blood of patients from California, Colorado, Idaho, Montana, Nevada, Oregon, Utah, Washington and Wyoming. To date there have been no cases reported from Canada, but it seems probable that the disease has occurred there, especially since the virus has been obtained from ticks harvested in Banff National Park.

Investigators have found that up to 14.3 per cent or more of *Dermacentor andersoni* harvested in endemic areas are infected with the virus of Colorado tick fever. Whether or not ticks other than *Dermacentor andersoni* harbor the virus remains controversial. Florio, Miller and Mugrage[18] reported the presence of the virus in dog ticks, *Dermacentor variabilis*, harvested on Long Island in 1950. However, Eklund and associates[1] in an extensive survey of various tick populations throughout the country were able to isolate and positively identify the virus of Colorado tick fever only once in ticks other than *Dermacentor andersoni*, and this in a sampling of *Dermacentor occidentalis* from Oregon. The manner in which Colorado tick fever is perpetuated in nature has not been worked out completely. Questions concerning transovarian infection[14] and natural animal reservoirs continue to be under investigation.

Incidence and Variations

The actual incidence of Colorado tick fever is difficult to assess. Mild forms of the illness

TABLE 1

CASES OF COLORADO TICK FEVER REPORTED TO THE UNITED STATES PUBLIC HEALTH SERVICE, 1947-1956

	COLORADO	OREGON	UTAH	WASHINGTON	WYOMING
1947	69				4
1948	67				
1949	117		3		2
1950	99	3			2
1951	39		1		9
1952	62	13			
1953	70	9	1	1	
1954	115	22			
1955	223	4			10
1956	107	22			3

doubtless are overlooked and not reported. Certainly most patients are not hospitalized. Subclinical forms of the disease occur,[19] but it is hard to determine their frequency. The illness has been reportable to the Colorado State Health Department during recent years. Table 1 lists the number of cases reported to the United States Public Health Service during the past decade. All these figures probably are far lower than the true incidence.

Recently developed technics for studying the virus and the immunologic behavior of Colorado tick fever have shown that the clinical pattern may vary. Some patients have a single episode of illness lasting a week or 10 days, while others have three or more remissions and exacerbations. There may be encephalitic or meningitic complications. The incidence of the latter is not known, but the problem of diagnosis is a significant one in the Rocky Mountain area where mosquito-borne encephalitides occur along with a number of other viral infections of the central nervous system.

Diagnosis

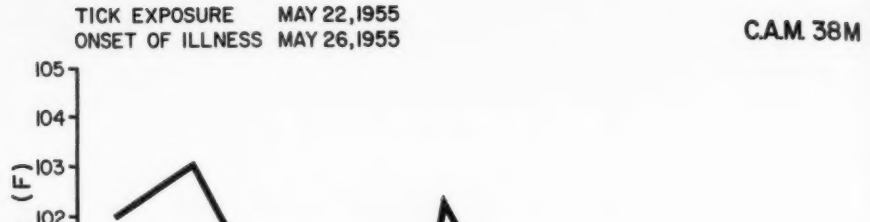
Diagnosis of Colorado tick fever in its characteristic form is not difficult. A careful history relating to possible tick exposure is most valuable in this respect. The course of the illness, absence of rash, and leukopenia help corroborate the clinical impression.

Dengue is the closest clinical analogue of Colorado tick fever, but the epidemiologic features of the two diseases are mutually exclusive. Immunologically the causative viruses are unrelated.[20] From a practical standpoint the differential diagnosis includes distinguishing the disease from the prodrome of Rocky Mountain spotted fever, abortive Rocky Mountain spotted fever, influenza, and infectious mononucleosis.

The rash of Rocky Mountain spotted fever usually does not appear until the third or fourth day of illness. Hence, after known tick exposure and during the prodromal period one might easily confuse spotted fever with Colorado tick fever. Further, early and aggressive antibiotic therapy of true Rocky Mountain spotted fever may abort the clinical course so that the rash does not appear and the overall illness is indistinguishable from Colorado tick fever. In such an instance the only unequivocal differentiating point would be demonstration of the virus of Colorado tick fever or *Rickettsia rickettsii* in acute-phase serum, or subsequent development of the appropriate antibody.

Influenza may have an onset similar to Colorado tick fever, and leukopenia may accompany it. Here, again, specific laboratory procedures are necessary to label the disease properly.

Infectious mononucleosis may have a rapid



WBC (THOUSANDS)			3.5	3.8	4.7	2.7	2.4	3.6
CTF								
VIREMIA	0	+	+		+	+	0	
NEUT.-INDEX	0							
C-F TEST	0							720 0

FIGURE 1 (case 1). Clinical course and laboratory findings in a typical case of Colorado tick fever.

onset, and leukopenia and splenomegaly may be features of the illness. The atypical cells of mononucleosis may be absent early in the disease, and some atypical lymphocytes may appear in the course of Colorado tick fever, particularly in young children. Sore throat and adenopathy may not be prominent features of mononucleosis. However, the course of the illness, follow-up of the peripheral blood picture, and development of heterophile antibody should establish the diagnosis of infectious mononucleosis.

Case Reports

We shall describe two cases briefly to illustrate, first, the prototypal illness and, second, a variant with a more complex picture, less easily recognizable on clinical grounds.

Case 1—Figure 1 illustrates the clinical course and laboratory findings in the case of a 38 year old surgeon who experienced the rapid onset of chilliness, retro-orbital headache, photophobia, general muscle aching, malaise, and a "metallic taste" in the mouth on May 26, 1955. Four days earlier he had been on a fishing trip in the Colorado Rocky Mountains. He had noted ticks on his body but had not found any attached. His symptoms progressed and excessive weakness developed. His temperature ranged from 101 to 103° F. for two days. The fourth day he was afebrile and felt sufficiently improved to show his Labrador retriever in a field trial. All his symptoms returned the next day and persisted for two more days. Rapid and marked improvement occurred on the next day and the subsequent course was uneventful, although convalescence was somewhat prolonged and marked by excessive weakness and mild apathy for several days.

Physical findings were within normal range throughout the illness except that the tip of the spleen was palpable 2 cm. below the left costal margin. The white blood cell count ranged from 2700 to 4,750 per cubic millimeter. The virus of Colorado tick fever was present in blood drawn on the second, third, fifth and sixth days of illness. Neutralizing anti-

body against Colorado tick fever was present on the sixteenth day after onset. Complement-fixing antibody had not developed at that time.

This case was quite characteristic of the usual clinical course of Colorado tick fever.

Case 2—Figure 2 represents the case of a 10 year old white boy who was transferred to the Colorado General Hospital from a private hospital on April 6, 1956. His illness began April 1, 1956, with sudden malaise, fever, sore eyes and headache. These symptoms persisted for two days and his temperature ranged between 102 and 103° F. His family physician treated him with antibiotics and aspirin. On the fourth day the patient felt quite well and went to school. However, he returned in the afternoon with a temperature of 103° F. and was sent to a private hospital where a markedly stiff neck was noted. Spinal fluid contained 90 cells per cubic millimeter (84 per cent lymphocytes), 96 mg. sugar per 100 cc., and 60 mg. protein per 100 cc. The white blood cell count was 3800 per cubic millimeter (49 per cent lymphocytes, 60 per cent monocytes, 35 per cent polymorphonuclear leukocytes).

The patient had been in the mountains a week prior to the onset of illness. Two days before the illness his mother noted a tick embedded in the skin between his shoulder blades. The family physician excised the tick.

When the patient was transferred to the Colorado General Hospital on the sixth day of illness, physical examination revealed an irritable child with slight injection of the right tympanic membrane and considerable injection of the sclerae and conjunctivae. There was no rash. The tip of the spleen was palpable, and the neck was moderately stiff. Otherwise, physical findings were within normal

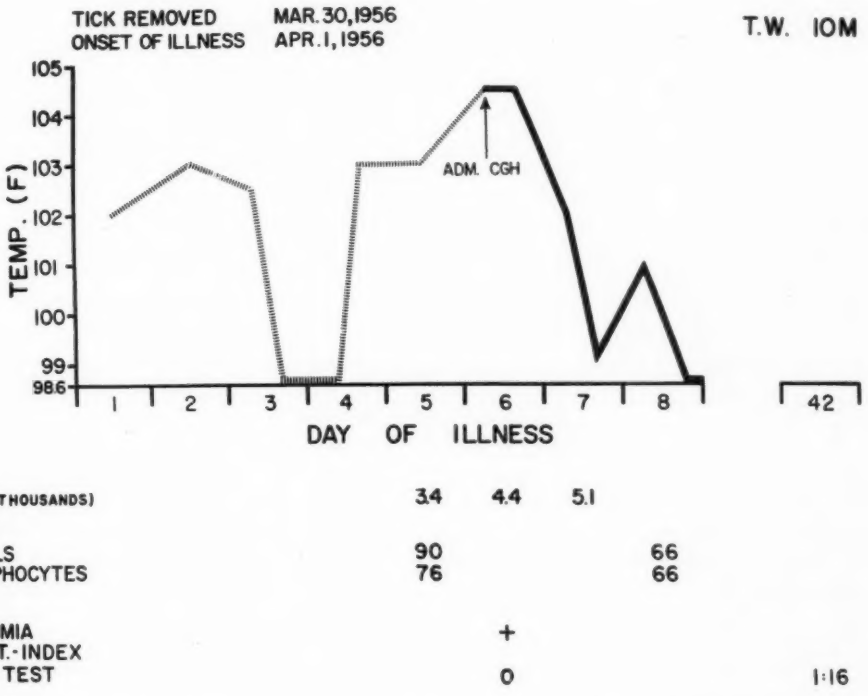


FIGURE 2 (case 2). Clinical course and laboratory findings in a case of Colorado tick fever that was less easily recognized on clinical grounds.

limits. White blood cell count was 4400 per cubic millimeter (50 per cent lymphocytes, 45 per cent neutrophils). Spinal fluid examination on the third hospital day revealed 66 white cells (all lymphocytes) and normal levels for sugar and protein. The patient was treated symptomatically with fluids and salicylate. He remained irritable and febrile for approximately 24 hours, after which he improved markedly and became afebrile and asymptomatic. He was discharged on the third hospital day. The virus of Colorado tick fever was grown from blood drawn on the sixth day of illness. Complement-fixing antibody was not present in the acute-phase serum initially but was present in a 1 to 16 dilution six weeks after the onset of illness.

Without the history of exposure to ticks, this case would have been considered a nonspecific viral meningitis. Spinal fluid was not examined for the virus of Colorado tick fever; it was undoubtedly present, however. Florio, Miller and Mugrage[17] obtained the virus of Colorado tick fever from the spinal fluid of patients who did not have meningitic signs or cells in the spinal fluid. It is possible that in the case just described the meningitic symptoms and the pleocytosis were due to a second, unrecognized disease. Other possible causes were not specifically excluded. However, the history of exposure to ticks, the demonstrated presence of the virus of Colorado tick fever, and the development of antibody against Colorado tick fever prove its presence unequivocally. To implicate a coincidental illness does not seem reasonable.

Discussion

Colorado tick fever does not appear to represent a serious threat to public health. However, each year the Rocky Mountains attract increasing numbers of tourists and sportsmen and the incidence of the disease may well increase. At present the illness itself does not warrant extensive and specific measures to control the tick population, but this might be accomplished in endemic areas. Further, specific immunization is potentially available. Koprowski and associates[21,22] developed an experimental vaccine, but the essentially benign and self-limited nature of the disease does not indicate its large-scale use at present. Certainly persons planning to enter areas which are heavily infested with ticks should be informed of the hazards and of appropriate personal precautions, including the wearing of proper clothing and careful inspection of scalp, neck, sleeve, belt, trouser and sock-line areas for ticks at frequent intervals. Finally, as Eklund and co-workers[1] pointed out, although the disease is contracted only in the Rocky Mountain area, modern transportation has been responsible for the appearance of Colorado tick fever in areas remote from the mountains, and physicians throughout the country should be aware of the clinical entity.

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Some Observations on Sunlight and Skin Cancer

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THE first reports suggesting sunlight as a cause of skin cancer were published more than 60 years ago. The idea caught on slowly, but judging from the numerous articles in recent literature there is keen interest in the subject at present. The volume of reports on experimental production of skin tumors by using ultraviolet light is increasing, and apparently clinical evidence of the same effect is accumulating.

It is now generally accepted that environmental factors play a large part in producing skin cancer. More cases are reported from areas of high altitude with clearer air and from the warmer coastal regions where people spend more time outdoors than from other areas.

It is also well known that racial characteristics are important. Persons who have milk-white skin, even with black hair, are quite susceptible. Thin-skinned blonds are even more susceptible, and red-haired freckled persons are the most susceptible to skin cancer. It would seem that the more deeply pigmented the skin the less proneness there is to skin cancer. Generally this is so, but thickness of the exposed epithelium may have an even greater role in protecting against the damaging rays.

The United States Public Health Service has gathered statistics on the incidence of skin cancer in a number of cities and states. Great variations were encountered in some areas, but generally more cases were found in the South than in the North, except for some localities of uniformly high elevation. One report[1] covering 10 large cities listed Denver as third from the top, with 122 cases per 100,000 white residents. Detroit had 24 cases of skin cancer per 100,000 population. Another report estimated that Colorado has a very high incidence, possibly exceeded only by Florida.

To one who has practiced dermatology for 30 years in Denver the evidence that sunlight is a major cause of skin cancer seems overwhelming. Day after day I see patients who have all the varying phases of weathering of the skin: in childhood, the different types of light sensitization; in older persons, repeated

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violent sunburn; in still older persons, chronic erythema solare; and later, the multiform changes characterizing senile skin. In these later stages premalignant lesions are continually developing, and eventually a certain number become typical epitheliomas. Over 90 per cent of these develop on the exposed skin, and by far the greater proportion of the patients are persons of the "outdoor type"—sportsmen, ranchers or those who spend their leisure or work hours out of doors in the clear air and sparkling sunlight so common in this area, where the elevation varies from 1 to 3 mi. above sea level.

Most of the experimental evidence that ultraviolet radiation causes cancer has come from studies using artificial sunlight, but natural sunlight in the so-called tanning range also has been employed experimentally. Blum,[2] in a recent article, attributed to Angel Roffo (1933) the induction of cancer in rats by exposing them to natural sunlight.

To my knowledge it has not been proved that fluorescent light is carcinogenic, but experiments have shown that it alters the susceptibility of the skin to later ultraviolet reactions. In one instance[3] fluorescent light caused recurrence of a polycyclic eruption on the neck of a light-sensitized Negro.

The artificial ultraviolet light used in the experimental studies of skin cancer produces rays in the range between 2,537 and 3400 A. There is considerable controversy as to how these rays exert their carcinogenic effects. Undoubtedly they affect the cells directly, but there is also ample evidence that they produce some chemical change indirectly, probably in the nucleus, and this chemical substance may be the carcinogenic agent.

Dr. Leonard Freeman, formerly a professor of surgery at the University of Colorado Medical School, stated that he thought skin cancer is more common on the face, particularly the nose, because of a higher level of tissue cholesterol in these sites. Scientific proof of this has not appeared in the literature as far as I can determine. Cook[4] speculated on the possible importance of cholesterol as follows:

"The rays of the sun may have a direct action on the cells; but it is at least possible that the action may be indirect and involve a photochemical conversion of some constituent of the skin into a chemical carcinogen. A substance which suggests itself in this connection is provitamin D, which is known to be converted into the vitamin by ultraviolet. Provitamin D is closely related to cholesterol and is, in fact, cholesterol from the molecule of which two atoms of hydrogen have been abstracted. Recent work has shown that, by some relatively minor variations in the conditions of irradiation, the photochemical transformation of provitamin D may take a different course and give rise, by a modification of the ring system, to a substance known as an anthrasteroid, which has a structure not far removed from that of a carcinogenic hydrocarbon of the benzanthracene group. To the chemical mind there is no difficulty in imagining photochemical conversion of provitamin D to a chemical carcinogen. But again I am being fanciful and am speculating about changes which might well take place but for which there is no direct evidence."

In discussing the indirect effect of ultraviolet radiation, some authorities point to nucleic acid as the villain. Kelner and Taft[5] stated: "A working hypothesis for ultraviolet carcinogenesis is thus: the first step in the change from a normal to a tumor cell is some alteration in the nucleic acid in the cell nucleus, resulting in change of some nuclear function."

From the experimental and clinical evidence it seems reasonable to state that sunlight is a potent factor in producing human skin cancer. It also seems reasonable that people should enjoy the outdoors. If they are sensitive to light, adequate protection is available. Premalignant lesions should be removed properly; and skin cancers too can be treated so successfully that man need not live his life in the gloom of perpetual shade.

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Antibacterial Drugs in the Prevention of Rheumatic Fever

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ACUTE rheumatic fever is a generalized inflammatory disease which is initiated by group A streptococcal infections and frequently results in chronic valvular heart disease. Although it may be considered a nonsuppurative complication of a specific bacterial infection, its onset characteristically occurs after the symptoms of the original infection have subsided, streptococci are not demonstrable in the affected tissues, and antimicrobial therapy will not curtail the disease process, once it is manifest. Various theories have been proposed to explain the relationship between streptococcal infections and rheumatic fever, but none has been substantiated, and it seems likely that definitive control of the disease itself must await elucidation of its pathogenesis.

Despite our present lack of understanding, however, the recognition of a distinct relationship between streptococcal infections and rheumatic fever does provide a sound basis for the prevention of the disease; namely, the prevention or early treatment of streptococcal infections. Considerable evidence has been accumulated in support of the concept that either the prevention of streptococcal infections or prompt treatment of an established streptococcal infection constitutes an effective means of reducing dramatically the incidence of acute rheumatic fever. Since these two approaches differ in several important respects, they will be discussed separately.

Prevention of Streptococcal Infections

The group A streptococcus is a ubiquitous organism, widely distributed in environmental deposits. It is a common pathogen for man, and, although it occasionally produces disease in animals, it primarily affects humans, chiefly causing upper respiratory infections such as pharyngitis, tonsillitis and otitis. Less often it may be identified as the causative organism in cellulitis, lymphangitis and pneumonia. Erysipelas appears to be decreasing markedly in incidence, and such group A streptococcal infections as meningitis, endocarditis and pu-

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erperal fever have almost vanished. Despite the widespread distribution of the organism, nonanimal sources are for the most part of minor importance in the spread of infection, the great preponderance of which results from air-borne transmission from one person to another.

Of historical interest only are methods by which control of streptococcal infections was attempted prior to the advent of the sulfonamides and later the antibiotics. Thus, isolation of scarlet fever patients, decontamination of the environment, tonsillectomy, bacterial vaccines, and a number of other methods were employed without significant curtailment of epidemics or decrease in individual susceptibility. Subsequent to the introduction of the sulfonamides, data were accumulated which clearly demonstrated that daily administration of one of these agents decreased significantly the incidence of streptococcal infections. These observations were greatly extended during and after World War II, and comparable observations regarding penicillin were added. It would be impractical to attempt to protect every person by means of daily drug administration, but when the risk of infection is high or when the individual probability of having rheumatic fever is increased, prophylaxis is advisable.

During epidemics of streptococcal sore throat, the institution of mass prophylaxis should be considered. Although the streptococcal disease rates in a community rarely warrant such drastic action, certain segments of the population may be more severely affected. This is particularly true in closed units such as schools, institutions and military organizations where there is intimate daily contact among individuals. Prolonged epidemic disease rates result, during which time a large proportion of the group may be affected. In such instances, the application of mass prophylaxis will result in immediate curtailment of the disease. Selection of the proper prophylactic agent is of utmost importance. The drug should be bactericidal for the streptococcus and it must be employed in sufficient dose-duration to eliminate carriers. If a nonbactericidal but suppressive drug is used, the epidemic will be temporarily controlled, but the disease may resume after prophylaxis is discontinued, since the contagious source of the streptococcus is not eliminated.

Following acute rheumatic fever, patients must be completely protected from further streptococcal infections which may reactivate the disease. Repeated rheumatic attacks are accompanied by a significant mortality and by an increase in the severity of chronic valvular heart disease. Furthermore, rheumatic individuals are more likely to have acute rheumatic episodes after a given streptococcal infection. The previously nonrheumatic patient's convalescence, following a streptococcal sore throat, is complicated by rheumatic fever in 3 to 5 per cent of the cases. In the rheumatic subject, however, the recurrence rate may approach 100 per cent in the first year following the disease, and the patient may continue to exhibit a higher degree of susceptibility for the rest of his life. The physician should not rely on the diagnosis and treatment of streptococcal infections as a means of preventing recrudescences of rheumatic fever, since the rheumatic process may be activated concurrently with the infection. Furthermore, in over 30 per cent of all streptococcal infections, symptoms are mild or nonexistent so that the patient may not seek medical aid.

From the foregoing discussion, it should be apparent that the rheumatic patient must have continuous, uninterrupted prophylaxis for an indefinite period. Prophylaxis should be maintained year around and should not be intermittent or sporadic. As to the duration, some indecision exists. It is generally agreed that following the acute rheumatic illness, the patient should be completely protected from infection for at least 10 years, or longer if he is unduly exposed to the streptococcus; some authorities recommend protection for life.

In the rheumatic subject, drugs that are suppressive to the streptococcus are usually adequate; or bactericidal drugs may be employed in suppressive doses. In either instance, before prophylaxis is instituted, the patient should receive a course of antibiotic therapy that can be expected to eradicate the streptococcus from his throat.

Both the sulfonamides and antibiotics have

TABLE 1

RECOMMENDED DRUGS AND DOSES TO BE EMPLOYED IN STREPTOCOCCAL PROPHYLAXIS IN INDIVIDUALS WHO HAVE HAD RHEUMATIC FEVER

DRUG	DOSE	DOSE INTERVAL	METHOD OF ADMINISTRATION
Sulfadiazine	1.0 gm.	24 hours	Oral
Penicillin G tablets	250,000 units	12 hours	Oral
Penicillin V tablets	250,000 units	12 hours	Oral
Benzathine penicillin	1,200,000 units	4 weeks	Intramuscular
Tetracyclines	250 mg.	12 hours	Oral
Erythromycin	200 mg.	12 hours	Oral

been employed in streptococcal prophylaxis. With some drugs, extensive knowledge is available as to effectiveness and toxicity whereas with others, information is incomplete so that the recommendations presented are less well founded. A summary of the recommended prophylactic drugs may be found in table 1.

Prophylactic Drugs

Sulfonamides—The sulfonamides were the first drugs employed in streptococcal prophylaxis and they have since been thoroughly investigated. These drugs are not bactericidal for the streptococcus, but they are capable of markedly suppressing the organism and will prevent infection from occurring. When sulfonamides are administered to an epidemic population, a dramatic decrease in streptococcal disease rates ensues. If prophylaxis is stopped, after a short interval the epidemic again resumes since the human carrier state is not eliminated. Even if prophylaxis is maintained indefinitely, the disease may reappear, due to the development of sulfonamide-resistant strains. For this reason, the sulfonamides have proved unsatisfactory in the control of *epidemics* by the group A streptococcus and the drug should not be used in this manner.

In the rheumatic subject, the sulfonamides are quite effective in the prevention of streptococcal infections. Resistant organisms are rarely a problem since such strains only appear when sulfonamides are widely employed for a prolonged duration in a larger, homogeneous population. When administered daily to patients who have had rheumatic fever, sulfonamides will reduce the incidence of streptococcal infections by more than 80 per cent. Failures of prophylaxis are rarely due to the drug but more to the patient's neglect in taking his medication.

All absorbable sulfonamides are probably equally effective and there is little to recommend one over another. Toxic reactions have been bothersome and may force cessation of the drug in as many as 10 per cent of patients. Such reactions usually occur during the first few months and consist of mild skin rashes or transitory leukopenia. Severe or fatal reactions such as exfoliative dermatitis, bone marrow failure and polyarteritis have been rare.

Sulfadiazine or a similar drug, in a dose of 1 gm. taken once daily, constitutes adequate prophylaxis against infection by the group A streptococcus in adults. For children weighing less than 60 lb., one-half of this dose may be employed. In all instances, the physician must thoroughly indoctrinate the patient in the importance of maintaining *continuous* prophylaxis and periodically re-emphasize this point.

Penicillin—Penicillin has also proved exceedingly effective in the prevention of streptococcal infections and has certain distinct advantages over the sulfonamides. The drug is bactericidal against the group A streptococcus and will, therefore, eliminate the streptococcal

carrier state if administered in sufficient dose-duration. Furthermore, the streptococcus is quite sensitive to the action of penicillin and drug-resistant strains are unknown. Finally, untoward reactions to penicillin are less common and usually mild. All things considered, penicillin is the most satisfactory agent in prophylaxis of group A streptococcal infections.

Experience with penicillin in curtailing epidemics of streptococcal sore throat has been limited. It appears, however, that if the drug is administered to the affected group for a period of 10 to 14 days, the disease rates will decline sharply and the carrier state will be eliminated so that the epidemic will not resume after prophylaxis is stopped. For these reasons, penicillin has been found to be the most effective drug in mass prophylaxis. In the rheumatic subject, the continuous administration of penicillin should provide complete protection against infection by the group A streptococcus. As in the case of sulfonamides, failures in prophylaxis are rarely due to the drug and are attributable for the most part to the patient not adhering to a rigid regimen.

A wide choice of penicillin preparations is available, some having distinct advantages over others. Obviously, for long-term prophylaxis, the shorter-acting parenteral preparations such as crystalline penicillin, procaine penicillin, and penicillin in oil are impractical and unnecessary. In general, two forms of penicillin have proved useful:

1. Oral penicillin—Tablets of potassium penicillin G are the most widely used preparation for prophylaxis of streptococcal infections. With a dosage of 200,000 or 250,000 units twice daily, this drug will protect the individual from infection. When administered for 10 to 14 days in this dosage, the organism will be eradicated from most of the carriers; however, if employed with this purpose in mind, a third daily dose should probably be added. The oral form of benzathine penicillin is equally effective but has no distinct advantages. Penicillin V (phenoxymethyl penicillin) may prove as effective as penicillin G in lower doses and at longer intervals, or in either instance, but until the experimental evidence is more complete, this agent should be employed in the same dosage as is penicillin G.

The penicillin preparations for oral use are as effective as other forms of the drug in preventing infection and in eradicating the streptococcus from carriers when employed in comparable doses. Their main advantages are the ease of administration and the low incidence of untoward reactions. The only practical disadvantage is that maintenance of the prophylactic state depends on the patient's cooperation in taking the drug regularly.

2. Benzathine penicillin—This form of penicillin has gained wide use because after a single intramuscular injection, low but prolonged blood levels of the drug result. The duration of action of the drug depends to a large extent on the dose administered. Considerable individual variation in this matter exists, but present data would indicate the following durations of significant penicillin blood levels after a single intramuscular injection:

300,000 units	7 to 10 days
600,000 units	14 to 25 days
900,000 units	18 to 30 days
1,200,000 units	24 to 40 days

The injection of benzathine penicillin is often accompanied by local pain and induration at the site of injection, particularly when larger doses are administered, and some patients may refuse the drug subsequently. There is some evidence which suggests that benzathine penicillin, given by the parenteral route, may be responsible for more frequent and severe untoward reactions in comparison to oral preparations. Such reactions subside despite continued penicillin blood levels and subsequent injections are usually not attended by adverse effects.

If the local and systemic reactions to benzathine penicillin could be ignored, this drug would constitute an ideal form of prophylaxis against the group A streptococcus. A single injection of as little as 300,000 units eradicates the organism from over 80 per cent of carriers and protects the individual from infection for 7 to 10 days. Larger doses will eliminate virtually all carriers and may afford protection for as long as six weeks. The primary advantage of benzathine penicillin over others, however, is that the prophylactic state

TABLE 2

RECOMMENDED DRUGS AND DOSES FOR TREATMENT OF STREPTOCOCCAL INFECTIONS

DRUG	DOSE	DOSE INTERVAL	DURATION OF THERAPY
Benzathine penicillin	600,000 units	Single injection	Single injection
Penicillin G tablets	250,000 units	8 hours	10 to 14 days
Penicillin V tablets	200,000 units	8 hours	10 to 14 days
Tetracyclines	250 mg.	6 hours	10 to 14 days
Erythromycin	200 mg.	6 hours	10 to 14 days

can be maintained with certainty.

Experience with benzathine penicillin is still sufficiently limited so that recommendations as to dosage are subject to revision. It seems clear, however, that the administration of 300,000 units of benzathine penicillin to an epidemic population would markedly reduce the disease rates. Although the duration of protection with this dose is short, the disease rates should subsequently remain low since most of the carriers are eliminated. In the rheumatic subject, the dose must be related to the frequency of administration. In general, it has been found that the 1,200,000 unit dose, administered at monthly intervals, provides adequate protection for virtually all patients. Smaller doses may be employed but necessitate more frequent injections. In any case, part of the responsibility for maintaining the prophylactic state reverts to the physician when benzathine penicillin is used.

Other drugs—There has been very little experience with the tetracyclines, erythromycin or other antibiotics in streptococcal prophylaxis. The only justifiable reason for their use is in the rheumatic fever patient who has manifested sensitivity to penicillin or the sulfonamides. In such an instance, tetracycline in a dose of 250 mg. twice daily, or erythromycin in a dose of 200 mg. twice daily is probably adequate.

Treatment of Streptococcal Infections

In the management of acute streptococcal infections, the aim of therapy should be the eradication of the causative organism. If the streptococcus is eliminated, the symptoms will be ameliorated, suppurative complications will be prevented, and, more importantly, rheumatic fever will not occur. Therapy that only suppresses the organism will relieve symptoms and prevent most of the suppurative sequelae; however, rheumatic fever will result in the usual attack rate of 3 to 5 per cent. For these reasons, the physician should employ those drugs which have been proved to eradicate the streptococcus.

Since penicillin, chlortetracycline, oxytetracycline, tetracycline and erythromycin have been given clinical trials in the treatment of acute streptococcal pharyngitis and all appear to be equally effective in eradicating the streptococcus, the choice is a matter of personal discretion with reference to toxicity, cost and convenience. Regardless of the drug used, there is one basic rule of treatment: *The drug should be given so that continuous blood levels are maintained for at least 10 days and preferably for 14 days.* Eradication of the organism depends on the duration of therapy rather than on the total daily dose. So long as bactericidal concentrations of a given drug are maintained, increasing the concentration does not increase therapeutic efficacy, the eradication rate being directly proportional to the duration of therapy. Thus administering one of the above drugs for 14 days, 10 days, 8 days and 5 days will eliminate the organism from almost 100 per cent, 90 to 95 per cent, 80 per cent and 70 per cent of pa-

tients, respectively. The usual recommended daily dose is satisfactory since the streptococcus is exquisitely sensitive to the action of all those listed (table 2).

Although general rules of therapy have been mentioned, it may prove useful to review each preparation more specifically:

1. Aqueous penicillin can be employed but has the obvious disadvantage of requiring injections of the drug every four or six hours. By reason of its inconvenience, this form of the drug may be dismissed as impractical.

2. Procaine penicillin, penicillin in oil and similar preparations are more convenient than the aqueous form, but also have been supplanted by other forms of the drug.

3. Benzathine penicillin is theoretically the preparation of choice for general use in the treatment of streptococcal infections. A single injection of 600,000 or 1,200,000 units will provide prolonged blood levels of penicillin and will eradicate the organism from over 95 per cent of the patients. The striking advantage of this drug is that one dose thus constitutes adequate therapy. The major disadvantages of benzathine penicillin have to do with the local discomfort at the site of injection and the probable higher incidence of allergic reactions. Commercial preparations containing combinations of aqueous penicillin, procaine penicillin and benzathine penicillin are no more effective than benzathine penicillin alone.

4. Oral penicillin in the form of potassium penicillin G is effective in a dose of 250,000 units every eight hours. When such therapy is continued for 10 days, it is 90 per cent effective in eradicating the streptococcus. If, however, the interval of therapy is increased to every 12 hours, decidedly inferior results may be expected as effective blood levels of penicillin occur only intermittently. As indicated in an earlier section, penicillin V (phenoxymethyl penicillin) may permit an increase in the interval between doses, but until this is a proved fact, it should be administered in the same manner as penicillin G.

5. Administration of tetracycline, chlortetracycline or oxytetracycline, in doses of 250 mg. every six hours, constitutes adequate therapy for streptococcal infections. Gastrointestinal toxicity is a potential disadvantage of each of these drugs, but one of them may be indicated for the patient who is sensitive to penicillin. Similarly, erythromycin, in a dose of 200 mg. every six hours, may be employed.

The sulfonamides have been given extensive trials in the therapy of streptococcal infections. The results uniformly show that such therapy, while alleviating symptoms and preventing suppurative complications, does not alter the attack rate of rheumatic fever. This is to be expected since the sulfonamides are merely suppressive and do not eradicate the streptococcus. *Therefore, the sulfonamides should not be used in the treatment of group A streptococcal infections.*

Other antibiotics such as chloramphenicol, bacitracin, carbomycin and ALBAMYCIN® may prove to be effective against streptococcal infections. In view of the large number of suitable agents available, these need not be used.

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The Current Status of Open Cardiac Surgery

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THE inner surfaces of the chambers of the heart are the last anatomic areas of the body to yield to safe direct-vision surgical intervention. In the past five years, two entirely different methods to achieve this have been developed to the stage of practical clinical application. Thus, today, no portion of the human body defies surgical exposure.

The implications of this accomplishment on the future treatment of various forms of heart disease are obviously great, since both hypothermia and cardiopulmonary bypass are only in their infancy in terms of application to the technical problems posed by specific disease states. Significant advances in surgical treatment of various forms of heart disease can be confidently expected for years to come.

At present it would appear that hypothermia is the safer of the two technics, but it also has stricter limitations. Since this method received clinical trial earlier, it is not surprising that it has achieved a slightly more mature state of development. This is not, however, to say some pump oxygenators may not soon equal or exceed it in terms of risk; it is to be hoped that both technics will soon be essentially without risk. I shall outline some experience with both methods, and indicate some of the problems yet to be overcome.

Hypothermia

Stimulated by the report of Bigelow and associates[1] in 1950, hypothermia has been and is at present under continuing investigation in the Halsted Laboratory for Experimental Surgery at the University of Colorado. It was early observed that general hypothermia was attended by a high mortality because of severe myocardial arrhythmias (especially ventricular fibrillation) and because of serious disturbances in the clotting mechanism. Extensive experimental and clinical observations over the past five years have essentially eliminated both these hazards. We feel that the risk of hypothermia per se, as currently employed in this clinic, is in the neighborhood of zero.

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TABLE 1

PROGRESSIVE INCIDENCE OF SIGNIFICANT CARDIAC ARRHYTHMIAS IN 265 CASES IN WHICH HYPOTHERMIA WAS USED

	FIBRILLATION	DEATH	STANDSTILL	DEATH
First 100 cases	15	12	7	1
Second 100 cases ..	8	4	1	1
Last 65 cases	1	0	0	0

The following details in the management of clinical hypothermia for cardiac surgery appear important in promoting the safety of the method.

1. The range of the lowest rectal temperature achieved is 30 to 32° C. Circulatory arrest is performed at this temperature.[2] This limitation in degree of hypothermia is extremely important.

2. Cooling is accomplished simply and by design by immersion in ice water. There appears to be some rationale in cooling the peripheral tissue ahead of the heart and other vital organs.[3]

3. Throughout the entire procedure, a deliberate respiratory alkalosis is maintained by hyperventilation.[4,5]

4. Throughout the course of the cooling, operation and warming, dextrose is administered intravenously. Evidence is increasing that intravenous nutrients have a beneficial effect on the myocardium in hypothermia.[6]

5. The first two units of blood used during operation are heparinized, having been freshly drawn in plastic bags. The presence of platelets, fibrinogen and other enzyme elements of the clotting mechanism, together with the absence of citrate, are considered helpful in avoiding the bleeding diathesis of hypothermia.[7] Transfusion is given freely because a low blood volume is poorly tolerated in hypothermia.[8]

6. A bilateral sternum-splitting incision is always used in order to achieve adequate exposure and allow proper positioning.[9]

7. Great care is taken to position the patient so that the cardiotomy is in the uppermost portion of the heart, thus materially reducing the risk of air embolism occurring in the coronary arteries.[10]

8. After the establishment of inflow occlusion to the heart the coronary circulation is perfused with 1 to 2 cc. of 1:4000 PROSTIGMIN® in order to slow the heart. The decreased metabolic needs of the slowly beating heart apparently are important in reducing the risk of ventricular fibrillation.[11-13]

9. The root of the aorta is always clamped (except in operations for aortic stenosis) to prevent coronary blood flow during occlusion. This helps avert coronary air embolism, maintains bradycardia, and diminishes the coronary return to the heart, thus insuring a dry operative field.[14]

10. The period of circulatory arrest must not exceed six minutes. If more time is needed to complete the procedure, the operation should be interrupted and the circulation restored. A second period of occlusion can then be instituted after an appropriate interval to complete the procedure. The principle of multiple short occlusions allows at least 10 minutes of safe intracardiac time.[15]

11. Warming is achieved by diathermy, which is a form of internal warming. There appears to be some rationale for rewarming vital internal organs before peripheral tissues.[3]

Careful observation of these considerations reduces the mortality rate of hypothermia itself to a level that is essentially negligible. For example, the incidence of serious cardiac arrhythmias in our series of patients is given in table 1. The incidence of disturbances in the clotting mechanism is given in table 2. It is clear that as the limitations of the methods and better control of the unusual physiology were learned the risk has steadily decreased.

TABLE 2

PROGRESSIVE INCIDENCE OF CLOTTING DISTURBANCES DURING OR AFTER HYPOTHERMIA

	BLEEDING	THROMBOSIS	DEATH
First 100 cases	4	2	6
Second 100 cases ..	3	2	5
Last 65 cases	0	1	0

TABLE 3

PROGRESSIVE MORTALITY FOR ALL PATIENTS UNDERGOING OPEN CARDIAC PROCEDURES DURING HYPOTHERMIA (180 CASES)

	DEATHS	
	Number	*Per Cent*
First 60 cases	12	20
Second 60 cases	6	10
Third 60 cases	3	5

In the last 65 cases, not a single death was attributable to either ventricular fibrillation or a disturbance of the clotting mechanism.

The effect of better over-all management of hypothermia on the mortality rate of open heart operations is seen in table 3. Of course, better selection of patients and improving technic with increasing experience may play a part in the trend of these figures, but irrespective of the relative importance of various factors it is gratifying that there has not been a single death among the last 41 patients undergoing bilateral thoracotomy and open cardiotomy during hypothermia.

In view of this experience, we feel at present that those open cardiac procedures which can be technically achieved in 10 minutes of direct-vision time should be done during circulatory occlusion under hypothermia, since the method itself is so safe.

The following diseases are examples of lesions for which the open operation is clearly preferable to blind technics and the procedure can be done adequately within the time limit.

1. Pulmonary valvular or infundibular stenosis occurring as a single lesion.
2. Atrial septal defect (secundum).
3. A combination of pulmonary stenosis and atrial septal defect (trilogy of Fallot).
4. Aortic stenosis.

Both valvular and infundibular pulmonic stenosis, occurring as isolated lesions, are readily amenable to plastic repair. The results of open intervention in restoring normal hemodynamics and obliterating the pressure gradient have been very satisfactory.[16] Since the mortality has been nil in this group, we now recommend operation to any young patient whose pressure in the right ventricle exceeds 70 mm. Hg, irrespective of whether or not he has had any symptoms relative to the heart. Table 4 shows our total cumulative experience with these two lesions. With the risk rate so low and the results so satisfactory following open operation during hypothermia, it seems unwise at this time to recommend either a closed procedure or use of the pump oxygenator, with its greater risk.

Atrial septal defect of the so-called secundum type is a lesion complicated by many associated variations. Aberrant pulmonary venous drainage into the right auricle, multiple septal defects, unusual prominence of the valve of the inferior vena cava, and associated patent ductus arteriosus all commonly participate in this malformation. With such complexities it seems hardly necessary to mention the superiority of an open technic for treatment. In spite of its variety it is uniformly possible to repair the lesion in such a fashion that the pulmonary veins are transplanted to the left side of the repair in less than 10 minutes of operating time. Table 5 outlines our experience with this operation. In view of the fact that the last 41 patients with atrial septal defect have undergone a curative procedure without mortality, we are currently extending our

TABLE 4

RESULTS OF DIRECT-VISION REPAIR OF PULMONARY STENOSIS DURING HYPOTHERMIA (INTACT SEPTA)

TYPE	CASES	CURED	IMPROVED	DEATHS
Valvular	34	32	2	0
Infundibular	4	4	0	0

TABLE 5

RESULTS OF DIRECT-VISION REPAIR OF ATRIAL SEPTAL DEFECT (SECUNDUM) DURING HYPOTHERMIA

	CURED	DIED
First 43 patients	36	7 (16%)
Last 41 patients	41	0

TABLE 6

RESULTS OF DIRECT-VISION OPERATION DURING HYPOTHERMIA IN TRILOGY OF FALLOT

CASES	OPERATIONS	TOTAL CURE	IMPROVEMENT	DEATH
16	18	6	7	3

indications for operation in young persons with this disease. We believe at present that all patients with atrial septal defect (secundum) should have operation when the diagnosis is established, irrespective of the presence or absence of symptoms, gross cardiac enlargement, or other objective findings. A major contraindication to operation is reversal of the shunt with consequent cyanosis. In this respect, therefore, the indications for surgery are essentially similar to those for patent ductus arteriosus.

The combination of atrial septal defect and pulmonary stenosis (trilogy of Fallot) presents interesting therapeutic problems. In 15 of our 16 cases the shunt preoperatively was right to left, and the patient was cyanotic, in some instances extremely so. Our initial impression was that if adequate relief of the pulmonic stenosis were achieved the atrial septal defect might close spontaneously. However, in some cases cyanosis has persisted while in others a conversion of the shunt to a left-to-right direction has resulted in cardiomegaly and even cardiac failure. Two of these earlier patients, therefore, have undergone a second hypothermic procedure to close the auricular septal defect. In our last four patients we performed a two stage curative procedure at a single session, first opening the pulmonary valve and then suturing the atrial septum at a second occlusion. Our cumulative experience with this malformation is seen in table 6. Some of the earlier patients with only a single stage may eventually need closure of the atrial septal defect. In six of the surviving patients the circulatory system has been restored essentially to normal.

More recently we have explored the possibility of transferring our technic for pulmonic obstruction to operation on the aortic valve.[17] Exposure of the ostia of the coronary arteries to room air did not prove a serious deterrent, as methods for avoiding coronary air embolism were developed. The risks of this procedure have proved to be largely technical, since the need for much greater care in avoiding regurgitation of the aortic valve following manipulation limits the operation and extends the operative time. Nonetheless, the results in a small series to date have been sufficiently satisfactory to warrant continuation of the technic. These results are shown in table 7. In our opinion the open procedure is so superior to the digital and blind instrumental technics previously available that operative intervention in rheumatic aortic stenosis is justified much earlier, before there is extensive calcification of the valve. In addition, it is suggested that congenital aortic stenosis is more common than generally supposed and that, whether the obstruction is valvular or subvalvular in position, open operation is indicated when left ventricular strain is present, with or without subjective symptoms.

Total Cardiopulmonary Bypass

Many lesions require much more operating time than that currently permitted by hypothermia. For these, the pump oxygenator using total cardiopulmonary bypass is the method of choice. The variety of oxygenators and pumps currently in use throughout the world attests to the fact that the best design for such an instrument has yet to be developed. The problems associated with total bypass are multiple. Blood procurement and crossmatching, rate of flow, type of pulse, adequacy of oxygenation and extraction of carbon dioxide, avoidance of air embolism, aberrations in me-

TABLE 7

RESULTS OF DIRECT-VISION REPAIR OF AORTIC STENOSIS DURING HYPOTHERMIA

	CASES	IMPROVEMENT	DEATH
Congenital			
Valvular	10	9	1
Subvalvular	3	1	2
Acquired	2	2	0

tabolism, difficulties in sterilization, protection of the formed elements of the blood, and avoidance of interference with the clotting mechanism are only a few. Moreover, all these difficulties are compounded with time; the longer the perfusion, the greater the risk of serious or fatal physiologic deviation. Thus the very essence of the need for pump oxygenation, a prolonged operative time, imposes a condition which raises the risk. We know of no pump oxygenator as yet which has a risk rate approaching that of hypothermia.

Our earlier experience with a bubble-type oxygenator was extremely unsatisfactory. Damage to the cells, disturbance in clotting, and diffuse cerebral damage presumably from multiple small emboli were associated with inadequate flow rates. For these reasons we turned to a screen-type oxygenator with roller pumps, a combination which had long been studied by Gibbon,[18] and was subsequently further refined by Kirklin et al.[19] After extensive laboratory trial, this instrument received clinical trial in 13 cases of advanced pulmonary hypertension associated with interventricular septal defect. In most instances it was possible to close the defect by direct suture, but in three it was necessary to plug the defect. One patient, undergoing operation for the second time, had profuse bleeding during and after heparinization. Her hemorrhagic diathesis eventually proved fatal. Another child died quite unexpectedly of heart block a few hours after operation. The other 11 patients have done well, but the effectiveness of the repair and its influence on the advanced pulmonary vascular disease remain to be studied. It appears that the pump oxygenator system we are using is adequate although still replete with danger as bypass is prolonged. It will remain the subject of continuing laboratory investigation. We intend to extend its use to more complicated lesions such as transposition and tetralogy and to continue work on its potential use in acquired valvular disease.

Summary

Our experience with the current methods available for open cardiac surgery is briefly reviewed. At present, after a broad experience, we consider hypothermia to be essentially without risk and therefore the method of choice for intracardiac procedures which can be accomplished in 10 minutes or less. Our screen oxygenator in association with roller-type pumps has proved adequate for total cardiopulmonary bypass. The risks of this instrument have not been thoroughly assessed, but application to a broader spectrum of intracardiac conditions seems justified on the basis of our early experience.

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The Sequence of X-ray Changes in Pulmonary Embolism and Infarction

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FOR some years physicians interested in chest disease have noted an apparent relative increase in pulmonary embolism, thrombosis and infarction. Israel,[1] in a succinct and provocative article entitled "The changing pattern of pulmonary disease," outlined some of the factors contributing to this increase, including aging of the population, the relative rise in incidence of cardiovascular disease, and the greater number of persons hospitalized. He also mentioned the more exact diagnosis resulting from control of diseases confused with infarction, such as pneumonia.

A lively literature exists in current journals covering such subjects as embolism of the pulmonary artery and its relation to cor pulmonale, the relation of the sickling states to thrombosis of the pulmonary artery, and many others emphasizing the diagnostic problems concerned. Yet one still encounters, both in the literature and in talking with other physicians, evidence of reliance on such discredited signs as the "triangular shadow" on the x-ray and emphasis on the relatively rare sign of hemoptysis before the diagnosis of pulmonary infarction is seriously considered. Less well appreciated is the occurrence of large occlusions of the pulmonary vessels without concomitant changes in the x-ray appearance of the lung parenchyma.

The x-ray changes in pulmonary embolism and infarction assume new importance because all aspects of thrombo-embolic disease are attracting greater attention. I believe that x-ray diagnosis of these conditions can be more accurate than is generally appreciated.

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FIGURE 1 (case 1). Radiolucency as an early sign of pulmonary embolism. X-ray of the chest of a 49 year old man, made a few hours after the sudden onset of pain in the left side of the chest on December 24, 1956, reveals a triangular area of radiolucency at the left costophrenic angle. Note that the *base* of the triangle faces the hilus, and not the apex as was formerly taught.

Poor Aeration of the Lungs (Expiration Film)

For some time in our department we have made inquiries when an x-ray of the chest suggested that the patient could not take a deep breath. Because this is such a common and nonspecific finding we have been somewhat hesitant to mention it. We were pleased, therefore, when authorities of the stature of Fleischner and his associates[2] indicated that it had alerted them too. To the radiologist it may be the first indication of pulmonary embolism. If the history lends any support to this diagnosis, or if the diagnosis remains obscure, he should

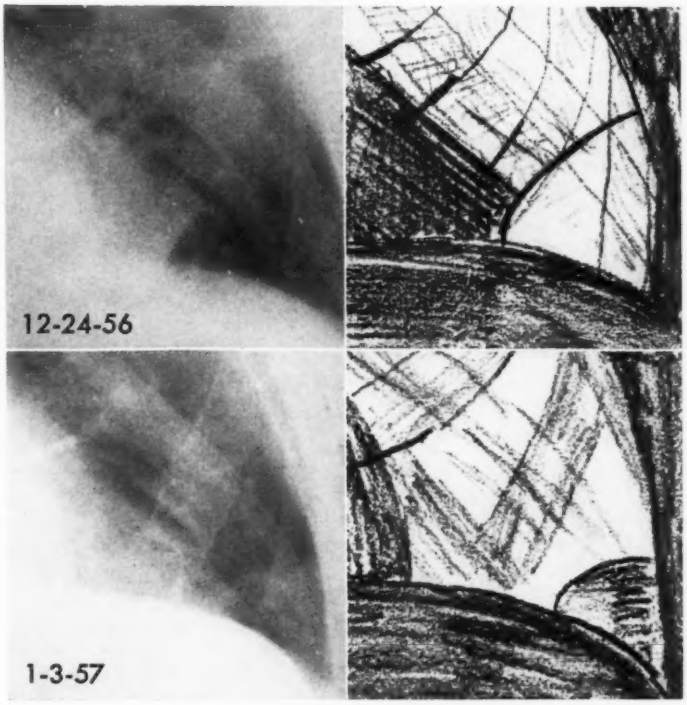


FIGURE 2 (case 1). Detail views of left costophrenic angle. December 24: Acute anemia due to embolus. January 3 (10 days later): "Hump-shaped" density much smaller than previous area of radiolucency. This appearance at the costophrenic angle is the most reliable single sign of infarct.

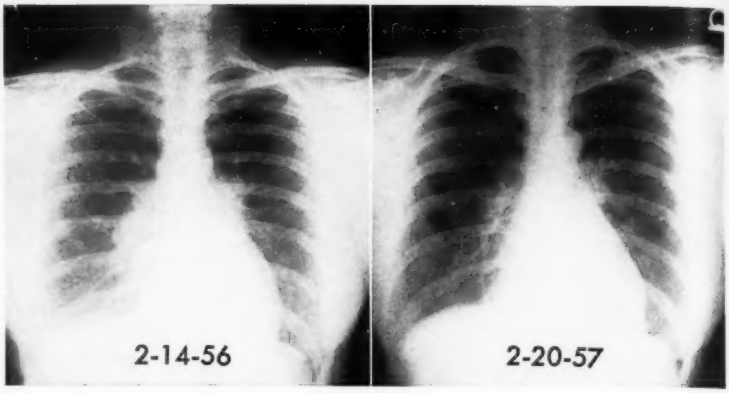


FIGURE 3 (case 2). *Left.* Chest x-ray of 49 year old woman who had a typical episode of thrombophlebitis of the left leg six weeks previously shows the "plump, tumor-like hilar shadows" described by Fleischner and associates. *Right.* One year later the appearance is more normal.

FIGURE 4 (case 2). Detail views of right hilus, February 14, 1956, and February 20, 1957. Patient was referred to Tumor Clinic.

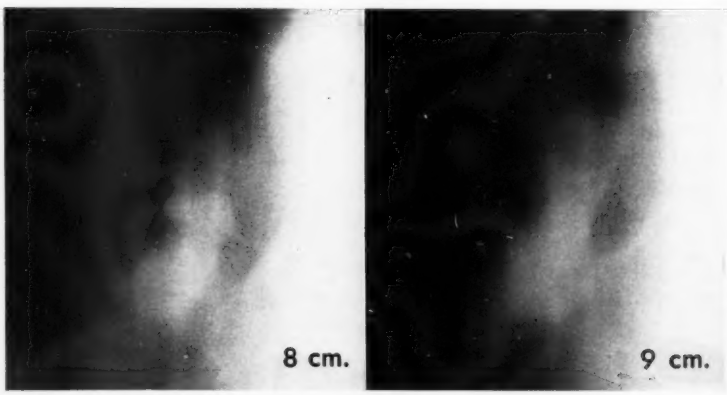


FIGURE 5 (case 2). Tomograms at 8 and 9 cm. levels were not very helpful. Angiography might have demonstrated occlusion. The shape of the fat, blunted right pulmonary artery is quite typical and reproduces the shape of the organized clot. Blood passes around the periphery of the clot.

FIGURE 6 (case 2). Normal bronchogram. Patient was followed for a year, and her symptoms gradually disappeared and the chest x-ray became normal.

request serial films at intervals of not more than two or three days.

Areas of Radiolucency as an Early Sign

In 1948 Westermark,[3] the eminent Scandinavian radiologist who has contributed much to the understanding of pulmonary embolism, said that immediately following pulmonary embolism the area of the lung peripheral to the block commonly appeared increasingly radiolucent as a result of anemia. Subsequent to his report many American radiologists almost became myopic looking for these lesions. By dint of much search most of them acquired one or two cases to be kept under lock and key for showing only to eminent visitors like Dr. Westermark. Figure 1 is an example of this phenomenon. It may be a common occurrence but, if so, it must be very transient for it is only rarely demonstrable on film.

Case 1—A 49 year old man who had intermittent precordial pain and electrocardiographic evidence of healed posterior myocardial infarct was admitted to the hospital on December 20, 1956, because of sudden pain in the left side of the chest, radiating to the left shoulder. Serial electrocardiograms did not show new changes and physical examination revealed only some splinting of the left side of the chest with some rales. A chest x-ray made on December 24 was interpreted as showing "minimal infiltration, left costophrenic angle." The patient was discharged with a diagnosis of "diaphragmatic pleurisy, cause unknown." On January 3, 1957, he was seen in our office, and a chest film revealed a typical "hump-shaped" infarct at the costophrenic angle (figure 2).

Engorgement of Pulmonary Vessels

Small emboli do not disturb circulation enough to cause changes in the hilar shadows, but larger emboli produce what Fleischner and associates[2] described as "plump, tumor-like hilar shadows." Serial films are needed to evaluate such changes, particularly when early films show that the patient is unable to breathe deeply. Usually the vessels return to nearly normal size in a few days, but in a few instances the embolus remains and only prolonged follow-up will provide the answer.

Case 2—A 49 year old housewife was referred to the Colorado General Hospital six weeks after a typical episode of thrombophlebitis of the left leg. Dyspnea on exercise, two pillow orthopnea, and dull pain in the right side of the chest with radiation to the right shoulder had developed. Examination did not reveal significant physical findings. Routine blood and urine studies gave normal results. Electrocardiographic findings were not remark-

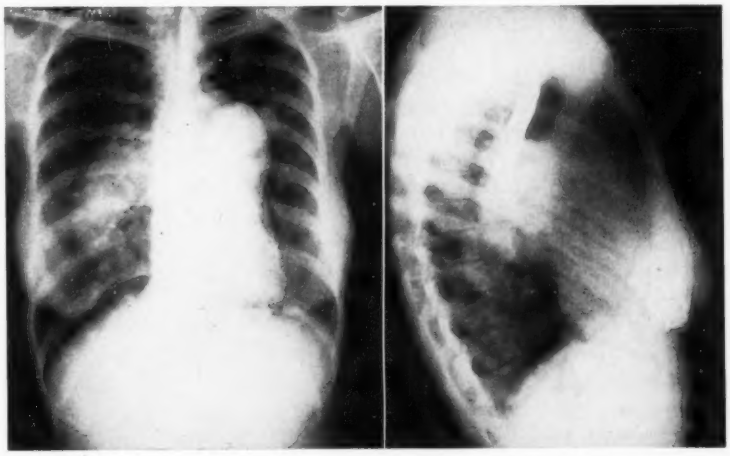


FIGURE 7 (case 3). Thrombosis of the pulmonary artery. The patient, a 30 year old woman, had many episodes of dyspnea. Peripheral lung fields appear anemic but there is little other evidence of parenchymal change. At autopsy a widely patent foramen ovale was found and the massive right pulmonary artery was filled with laminated thrombus, much of it old.

able. On a chest x-ray the right hilar shadow was thought to be enlarged (figures 3 and 4). She was admitted to the hospital, but tomograms (figure 5), bronchoscopic examination, and bronchograms (figure 6) did not yield a diagnosis. The patient was referred to the Tumor Clinic for follow-up. One year later, a chest x-ray was normal (see figure 3). The patient's symptoms had gradually disappeared.

In retrospect, a pulmonary embolism occurred at some time in the six weeks before the patient was seen at the hospital. The remainder of her work-up was done during a two month period when no changes appeared in the films. The fat, blunted right pulmonary artery is quite typical.

Pulmonary Embolism Without Infarction

The case just described illustrates that embolism can occur without infarction. Experiments show that it is very difficult to produce infarcts in normal lung, and there is reason to believe that if infarction does occur there is usually pulmonary disease or abnormality of the pulmonary circulation. Hanelin and Eyler[4] included among the changes occurring in thrombosis of the pulmonary artery right-sided enlargement of the heart (with or without right-sided failure), enlargement of the hilar contour (the outline of the hilus is essentially that of the thrombus), smaller than normal vessels distal to the thrombus, and a more radiolucent lung in the area normally supplied by the occluded vessels.

Case 3—A 30 year old woman had had increasing dyspnea and fatigability for nine years, and two years prior to admission to the hospital hemiplegia had occurred transiently. A chest x-ray (figure 7) disclosed massive enlargement of the main and right pulmonary artery, right ventricular enlargement, and relative ischemia in the peripheral lung fields. A few days after admission, severe dyspnea and precordial pain occurred suddenly and the patient died. At autopsy the right pulmonary artery was massively enlarged and almost completely occluded by laminated thrombus firmly attached to the wall of the artery. Microscopic and gross sections showed much old organized thrombus with some fresher premortem clots. The shape of the thrombus corresponded to the x-ray appearance of the vessel. The foramen ovale was widely patent (3.5 cm.).

Although the patient may have had infarcts in the past, it is interesting to note the relative clarity of the lung fields. There were no major areas of infarction at autopsy.

X-ray Sequence in Pulmonary Infarction

In a classic study reported in 1940 Hampton and Castleman[5] made the basic contribution toward an understanding of pulmonary infarction by correlating the x-ray changes with the gross and microscopic pathologic findings. Although they established without doubt that an infarct may assume any shape and that the "triangular shadow" with the apex pointing toward the hilus exists only accidentally as a superposition of multiple infarcts, their work indicates that *given serial films* and an understanding of the basic pathologic changes a fairly consistent pattern of change in pulmonary infarcts is often recognizable. Figures 8 through 12 illustrate these serial changes.

Case 4—A 45 year old Spanish-American man was thought to have poliomyelitis, and later the diagnosis of amyotrophic lateral sclerosis was considered. On October 2, 1955, while in the hospital, he had sudden pain in the left side of the chest with radiation to the left flank and shoulder, made worse by coughing and inspiration. His pulse and respirations increased and his temperature was transiently elevated. Dullness and rales appeared in the left side of the chest with splinting of the left hemithorax. This was the first of many attacks prior to his death the following year.

The usual pathologic sequence in pulmonary infarction is as follows: In 12 to 24 hours there is an outpouring of fluid into the alveoli, followed by some necrosis of the alveolar walls. During the first week or 10 days the margins of the lesion are poorly defined. Whether or not pleural effusion develops depends on many factors such as the presence of a free pleural space, amount of free pleura involved, and presence of concurrent pulmonary edema or left-sided heart-failure. There

FIGURES 8 to 12 (case 4). Typical sequence of films in pulmonary infarction.

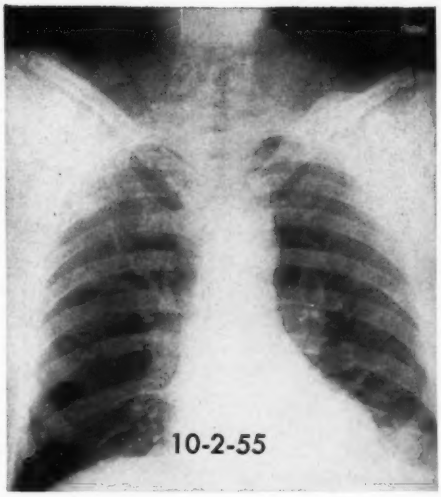
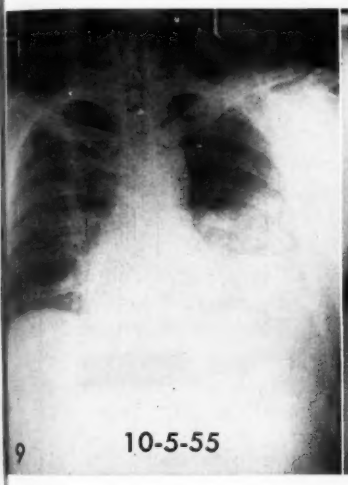


FIGURE 8. October 2, 1955. A 45 year old man had sudden pain in the left side of the chest, flank and shoulder a few hours before this film was made. Embolism probably occurred asymptomatically one or two days earlier. Density at the left base corresponds to the outpouring of exudate into the alveoli. Hilar shadows and lung vascularity cannot be evaluated accurately without serial films, but the hilar shadows are certainly prominent.



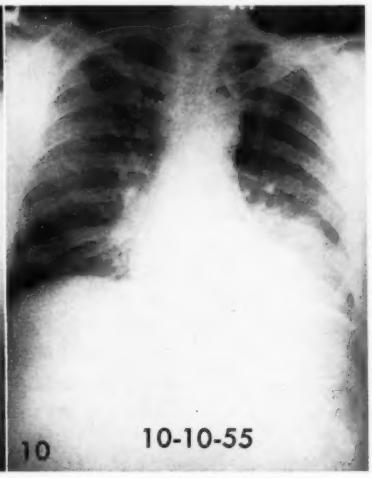


FIGURE 9. October 5, 1955. Extensive pleural involvement (suggested by initial symptoms) has resulted in a large pleural effusion on left, obscuring parenchymal infiltration. Patient unable to take a deep breath, and expiration films accentuate vascular engorgement on the right.

FIGURE 10. October 10, 1955. The pleural effusion is absorbed rapidly and parenchymal lesion is again seen. The involved area appears larger than it did on October 2. Effusions of this size in antibiotic-treated pneumonia are rare. Contralateral lesions (not seen in this case) are frequent and are strong evidence for infarction.

FIGURE 11. October 19, 1955. The margins of the infarcted area are sharper. The bordering area of "incomplete infarction" has resolved without necrosis and the increased clarity of outline represents the border of necrotic tissue; pathologically, granulation tissue is growing in at the margins. Pneumonia tends to clear much more uniformly.

FIGURE 12. November 28, 1955. Eight weeks after onset the infarcted area is somewhat more opaque than the remainder of the lung. There is a linear scar, which is commonly the only residual of infarction. Small infarcts heal much more rapidly than large ones.

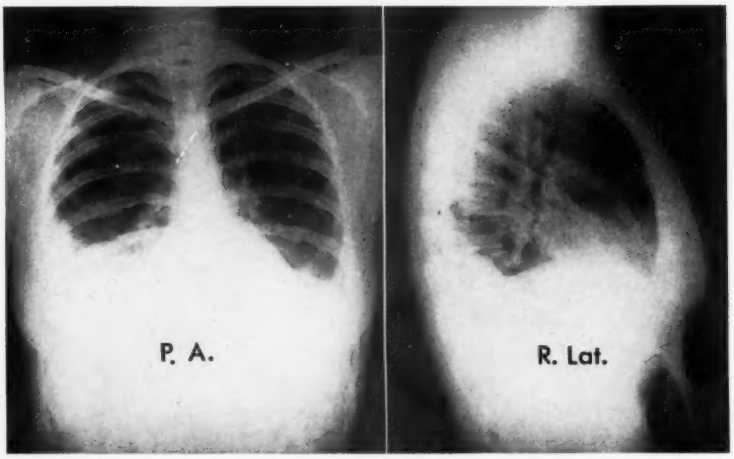


FIGURE 13 (case 5). Hump-shaped infarct at right base. Compare with figure 2 showing infarct at costophrenic angle.

may be a large amount of fluid in the pleural space, and if the patient first consults a physician at this stage and if the embolus has been relatively asymptomatic the diagnosis may be missed. Organization begins in the second or third week and the x-ray shows clearing at the periphery with much improvement in definition of the margins. Further healing depends to some extent on the size of the lesion. The end result may be a completely clear lung but frequently there are rather coarse linear scars (figure 12).

The Most Reliable Single Sign of Pulmonary Infarction

When Hampton and Castleman[5] discredited the "triangular shadow" with the apex pointed toward the heart as a sign of infarct they supplanted it by pointing out that in certain cases of pulmonary infarction, particularly at the costophrenic angle, there is a triangular density with the apex pointed *away* from the hilus and a "hump-shaped" convex border on the side toward the heart. An example of this already has been described (case 1, figures 1 and 2).

These hump-shaped densities occur elsewhere in the lung but are usually overlooked because they are not as easily seen as they are in the costophrenic angle.

Case 5—A 30 year old housewife underwent cesarean section on August 28, 1955, because of placenta praevia. For five weeks prior to operation she had been kept at bed rest. She was dismissed from the hospital on September 5, and that afternoon she experienced gradually increasing pain in the chest, pleuritic in type, without cough or hemoptysis. An x-ray of the chest made on September 6 (figure 13) shows a hump-shaped density in the right posterior gutter. The patient was given anticoagulants and the symptoms have not recurred.

Figure 13 might easily be interpreted as representing pleural effusion, but the history and physical findings in the case point strongly to a diagnosis of infarction.

Pleural Effusion in Infarction

In 1948 Moberg[6] reported two small series of cases, one of "clinically typical" pulmonary infarction and the other representing pneumonia. He found that pleural effusion "dominated" the x-ray picture in half the cases of infarction, whereas in pneumonia the parenchymal disease "dominated" the picture 85 per cent of the time. Other authors refute his findings or fail to mention them. Certainly effusion is rare in virus pneumonia and large effusions are not common in antibiotic-treated bacterial pneumonia. Effusion occurring after infarction is absorbed rapidly even if the chest is not tapped, and this may account for the relative infrequency of the finding at autopsy. It is our impression that large effusions are

common *at some time in the course of evolution of the infarct,* usually during the second week, and we agree with Boyd and Nightingale,[7] who said: "The diagnosis of pleural effusion . . . should be regarded with distrust until the presence of a pulmonary embolism has been excluded." This applies to medical as well as surgical patients.

Discussion

For many years clinicians have been aware of the gross inaccuracy of diagnosis of pulmonary embolism and infarction. Many autopsy series have shown that as many as 80 per cent of cases are missed clinically. In most instances the patients have signs and symptoms of infarction and the diagnosis is overlooked because it is not considered. Almost always the diagnosis of pneumonia or heart disease is made. In patients with heart disease one must always keep in mind the possibility of infarction, particularly when they fail to respond properly to treatment. Most cases of infarct and pneumonia should be distinguishable on the basis of the clinical history and laboratory findings alone, provided the patient is seen shortly after the onset of symptoms. If fairly frequent serial x-rays are taken one will note that infarcts seem to persist longer, that pleural fluid frequently accompanies them, and that they tend to demonstrate spread or contralateral involvement in the face of adequate antibiotic treatment. Pneumonia tends to clear sooner and more uniformly throughout the infiltration, whereas infarcts clear somewhat at the periphery with prolonged persistence of a central area.

Summary

The following x-ray changes tend to occur sequentially after pulmonary embolism and thrombosis:

1. No change may be observed in small occlusions.
2. Failure of the patient to breathe deeply.
3. Engorgement of the pulmonary vessels at the hila.
4. Ischemia of the lung fields peripheral to the occlusion.
5. Pulmonary infiltration, when infarction ensues.
6. Peripheral clearing of infiltration, with margins of necrotic areas becoming well defined at about the third week.
7. Pleural effusion, which may possibly be prominent.
8. Appearance of new areas in spite of antibiotic treatment.
9. Usually prolonged healing; healing may be complete or result in coarse linear scars.

These changes can be observed by careful radiographic examinations.

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Differential Diagnosis of Conversion Reactions in a General Hospital

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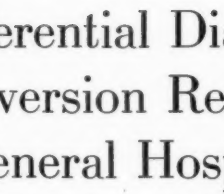
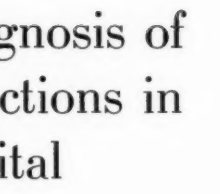


JOHN L. LIGHTBURN



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CONVERSION reactions are still seen in the offices of private practitioners and in hospitals and clinics in such numbers as to merit the constant interest, attention and awareness of physicians. Their prompt recognition and management are essential, lest the symptoms become fixed by extensive and repeated diagnostic and therapeutic procedures unrelated to the psychic etiology. Similarly, unduly deferred treatment may cause much direct and indirect suffering, incapacity and privation to the patient and his family.

Hysterical Character Disorder

Commonly, conversion symptoms occur in persons who have a type of personality or character described as hysterical. But not all persons of this personality type have conversion reactions that claim clinical attention.

Persons who have a hysterical character manifest a high degree of suggestibility and ready inclination to excessive fantasy and mendacity. They are often overdramatic in relating their histories, symptoms and relationships with other people. Dating of significant events is generally vague, and partial amnesia for the past is common. There is a good deal of emotional lability, readily recognizable as

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varieties of disproportionate fearfulness, i.e., anxiety. Despite the appearance of intense affect there is frequently an emotional shallowness in interpersonal relationships associated with instability and lack of satisfaction. Patients may express thoughts and feelings by overly inhibited or excited activity and are seldom inclined to moderate such behavior by reflection. An example of their suggestibility is their attachment to physicians, whom they tend to idealize beyond reason in ways that are reminiscent of erotic interest or childish dependency.

Persons with these personality traits are particularly prone to the development of conversion hysteria. We should stress, however, that when the symptoms of conversion hysteria do appear these characterologic manifestations tend to become clinically obscure.

Although the hysterical character disorder is a clinical psychiatric entity classed among the neuroses, it can and does occur in persons who for other reasons may be diagnosed as psychotic. Hysterical manifestations and psychoses are not mutually exclusive.

Conversion Reaction

Conversion reactions tend to take on certain forms, but they can directly or indirectly involve any organ or tissue and may simulate every known functional disturbance. The disturbance of function may be localized as with blindness, blocking out one sensory modality, or it may be widespread as in syncope, where all awareness of mental activity and of action is suspended. One or several organ systems may be involved, their functions may be changed in the direction of overactivity or underactivity, and the symptoms may be continuous, intermittent or episodic. If continuous (e.g., hysterical paralysis), secondary organic conditions such as contractures and atrophy may occur.

The pattern of symptoms does not correspond to the laws of anatomic and physiologic innervation. Rather, it corresponds to the patient's idea of disease and is related to the function which is increased, decreased or qualitatively changed. A paralysis will consist of the loss of a particular purposeful movement, often involving an entire limb, rather than being limited to a muscle or to the distribution of a single nerve. Further, the patient's attitude toward the affected part and its activity determines the distortion of function. Neurohumoral factors tend to play a negligible role. For example, a patient thinks of the hand as a part of the body that touches, explores and manipulates objects for emotional reasons, and rarely as a complex of nerves, bones, muscles and blood vessels. Similarly, anesthesias of the hand are typically of the glove type rather than being limited to the distribution of a peripheral nerve. The affected hand is the part of the body distal to the wrist.

When a conversion reaction is predominantly in the mental sphere it usually takes the form of dissociative reactions. These include such phenomena as amnesias, somnambulism, multiple personality, fugue states, dream states and stupors. With the exception of stupors, patients with such manifestations are not likely to be admitted to general hospitals. These symptoms are disturbances of consciousness, and only parts of total psychic functioning tend to be affected. For example, memory loss or amnesia is for a particular period or for a given group of experiences.

Pain also may be part of the conversion reaction. It is of two types: (1) "painless pain," a subjective response to the loss of function, which may be thought of as painful, and (2) pain correlated with physiologic dysfunction such as a spasm or cramp. Hysterical pain differs from physical pain in that the latter commonly is not continuous and if it is prolonged it exhausts and depletes the patient. Insomnia, if present, is independent of hysterical pain.

A major characteristic of the conversion reaction is the calm, anxiety-free mental attitude—*la belle indifference*. Physicians are often impressed with the patient's unexpected lack of concern over a conversion symptom that has catastrophic implications, such as blindness or paraplegia.

The onset of a conversion reaction usually is sudden and dramatic. Although the setting is often a stressful situation of psychologic significance, the patient represses these circumstances and the physician cannot easily elicit

them by direct questioning. Mass conversion reactions may occur in response to great catastrophes such as earthquakes, floods and bombings. The conversion symptom sometimes exploits a pre-existing injury or disease.

Differential Diagnosis

Differential diagnosis of conversion reactions can be a challenging personal issue to clinicians in general hospitals. Certain physicians frequently must cope with their tendency either to overlook the disease or to overreact to it. A suspicion of the existence of a conversion reaction may impair the diagnostic search for organic disease. Similarly, a disinclination to acknowledge the possibility of conversion reaction may lead to expensive and needless examinations that have no bearing on the disease under consideration.

The diagnosis of a neurotic disorder should not be made on the unidentified residue after relevant organic possibilities have been excluded. An adequate and reasonable physical, neurologic and laboratory examination and a psychologically perceptive medical history often are all that is required. At times the nonpsychiatric clinician considers an adequate psychiatric history onerous. To obtain a detailed account of the patient's life from his birth to the onset of his illness can be a formidable but unnecessary task. The regularly taught medical history can and should provide sufficient information to enable the thoughtful clinician to come to some conclusion about the presence or absence of a psychopathologic state. Indeed, with a few additional inquiries into certain important areas one may even draw some tentative conclusions about the nature of the disorder.

Medical history—A good medical history usually yields some strategic information about (1) the patient's social adjustment, (2) economic adjustment, (3) psychosexual adjustment, (4) past history of somatic illnesses and his reaction to them, and (5) overt neurotic or psychotic disorders. With respect to social adjustment a few questions need be asked to determine the number of his friends, the depth of his relationships, the manner in which he reacts to people, and how people react to him. Observation of his reaction to hospital personnel and the response that he elicits in them frequently will provide some of this information. Clues to his economic adjustment can be found in his employment history. How many jobs has he had? At what age did he become financially independent? Is his financial situation consistent with his training and ability? In the area of psychosexual adjustment one gets important clues by making simple inquiries into his marital history: age at marriage, age of the spouse, number and duration of the marriages, number of children, and degree of sexual compatibility. In taking a history of past illnesses only a few additional questions will reveal how the patient reacted to them and how long he was ill. Was the disability appropriate to the severity of the illness? Did illness occur at a time of psychologic stress? Finally, were there symptoms suggesting a neurotic disorder? We would hasten to add that the presence of positive findings in any of these five categories does not in itself confirm the diagnosis of conversion reaction. Rather, these findings simply inform the physician that there is some measure of psychopathologic disorder and indicate areas for further investigation. The physician who routinely assembles the data of his examination so as to inform himself about these five areas will be richly rewarded without being burdened.

Differentiation from secondary gain symptoms—A number of factors are operative in the choice of symptoms. One is that a conversion symptom will readily utilize an area in which constitutional weakness or acquired disease has lowered "resistance." The alert physician should think of this when, for example, he is puzzled by objective improvement without concomitant and corresponding symptomatic improvement. One should not confuse this with the secondary gain that symptoms sometimes provide patients. The typical manifestations of secondary gain can be observed in the "compensation case" in which symptoms are monetarily useful, or in the phobic patient whose panic and disabilities compel compliance and submission from persons around him. Symptoms retained for secondary

gain provide an escape from an uncomfortable reality but do not solve an unconscious, intrapsychic conflict. At times a conversion symptom will be associated with secondary gain, and this situation may present a difficult problem both diagnostically and therapeutically. Here the patient usually has additional psychopathologic disturbances above and beyond hysteria.

Differentiation from malingering—Diagnostic difficulty may also arise in distinguishing between conversion reaction and malingering. Unlike conversion reaction, or secondary gain, for that matter, malingering is a completely conscious attempt to imitate some pathologic process as a means to achieve a goal. The malingerer usually makes a great deal of noise about his symptoms, demands a lot of attention, and manifests concern about his disability. This is in contrast to the usually indifferent attitude toward the symptom in conversion reaction. Malingering usually is seen in persons who have a sociopathic personality disorder, that is, persons who characteristically do not suffer from any strong sense of guilt, who live primarily by the pleasure principle with little regard for the welfare or rights of others. Malingerers sometimes can be tricked out of their symptoms, whereas such devices do not affect the hysterical symptom.

Differentiation from psychosomatic diseases—There is a group of diseases customarily classed as psychosomatic whose prognostic and therapeutic implications necessitate a distinction between them and the conversion reactions. Here a psychogenic factor influences the onset, course and remission. Typical examples are hypertension, asthma, peptic ulcer, thyrotoxicosis and ulcerative colitis. This nosology is the consequence of usage and does not negate the principle that psychic factors influence all disease. Prevailing emotional states can decrease or intensify the psychosomatic disorders. A differential point that is sometimes misleadingly used is that conversion reactions are primarily found in the voluntary systems while psychophysiologic disorders occur primarily in the involuntary or vegetative systems. The many exceptions to this notion render it unreliable as a differential point. One must rely on an evaluation of character structure, the circumstances surrounding the illness, past history, and the presence or absence of anxiety to differentiate conversion from somatization.

Differentiation from hypochondriasis—Hypochondriacal symptoms are also confused with conversion reactions. In hypochondriasis the patients are intensely preoccupied with bodily functions and have unmodifiable, disproportionate concern over real or delusional alterations in one or more of these functions. Such patients have little interest in their environment, have multiple complaints, rarely will talk of anything but their symptoms, frequently complain of fatigue and lassitude, and insist that something be done about their symptoms (in contrast to the lack of concern about symptoms in conversion reaction). Hypochondriasis may be seen in anxiety reactions, in compulsion neurosis, and in a psychosis.

Anxiety in conversion reactions—We will make one final point about the diagnosis of conversion reactions. Thus far we have emphasized the presence or absence of anxiety as a basic consideration. Under special circumstances one may observe a form of anxiety in the presence of conversion symptoms. The conversion relieves the anxiety produced by the specific conflict. However, anxiety resulting from threatening external circumstances can be observed in these patients. For example, conversion symptoms may bring about the loss of a job. As a result the patient will be anxious about the consequences of the symptom but not about the symptom itself or about the conflict it symbolizes.

Report of Cases

Case 1—A 44 year old married, childless white woman who had had tuberculosis was admitted to the hospital for evaluation of the suitability of decortication of the lung because of persistent dyspnea and radiologic evidence of a markedly thickened pleura. She was described in conference as a former alcoholic.

In 1954, fatigability, a productive cough, night sweats and weight loss developed. A tuberculous-appearing lesion was noted in the right lung on a roentgenogram. The sputum

was positive for tubercle bacilli. In 1956 a pleural effusion in the right side of the chest complicated her disease, and it was aspirated repeatedly. Extensive pleural thickening developed. Because of her complaints of continuous shortness of breath and consequent fear of exertion, decortication of the lung was considered. The patient was studied by the medical, surgical and psychiatric services. The following physical and laboratory findings are of interest.

Findings on initial physical examination were primarily limited to the right side of the chest. A large area of dullness and decreased fremitus was noted over the lateral chest wall. The right diaphragm was high and its excursion somewhat decreased. Nevertheless the patient moved the right hemithorax well on fluoroscopic examination. She could hold her breath easily for more than a minute, and when engaged in a conversation was able to climb three consecutive flights of stairs without apparent exertional dyspnea. Pulmonary function tests produced results in the normal range. Roentgenographic examination revealed moderately advanced pulmonary tuberculosis with a loculated hydrothorax on the right, but the pleural effusion in the posterior portion of the chest was significantly decreased compared with the x-ray findings during previous hospitalizations. In view of these observations there was some doubt concerning indications for decortication, because of the lack of evidence that the thickened pleura was associated with physiologic respiratory limitation sufficient to cause the disabling symptoms.

To help explain these confusing findings, psychiatric examination was undertaken. A brief summary of this examination follows.

She was born on a farm, the second of four girls, to parents described as good people. The mother was a quiet, reserved, hard-working, nervous person who had many crying spells. She did not prepare her daughters for menses or, in fact, for any sexual functions. The patient consciously preferred the father; she considered herself the boy of the family and was closer to him than were her sisters. She worked on the farm with him and tended to identify with his interests and needs. He was a religious, authoritarian person, a good provider within the limits of his ability. Generally speaking she had a rigid, moralistic, judgmental upbringing.

During childhood she was very ill on two occasions with scarlet fever and diphtheria. She recalled how much extra attention she received at those times. She regarded herself as a nervous child since the age of four, being plagued by various fears. These included fear of high places and of being closed in a small room. She was intermittently afraid of a dark room, and during her recent illness her fear returned. She was always frightened of violence and rarely expresses anger directly. She had occasional dreams which she could not remember except that she experienced a sudden nightmarish waking with the sense that something "horrible" had been committed by or against her.

In adult life there was an unhappy teen-age marriage to an irresponsible, selfish and indifferent man which terminated in divorce when she was 25. Four years later she remarried; her husband was a man whom she liked but who, because of low back disease, subsequently became generally helpless and dependent on her. She was sexually frigid and had never been pregnant. Her life tended to be organized around her phobias. For example, she probably continued to support her husband in order to have him around to protect against her anxiety. She had frequent insomnia, nervousness, pain in the chest, and severe recurrent headaches. These symptoms increased in 1951 after her mother's death from carcinoma of the stomach and she began to wonder if she, too, had cancer of the stomach. Because of these symptoms she began to drink, thus giving rise to the alcoholism already mentioned. Progressive loss of appetite, weight loss and general diminution of resistance followed, and she felt these were strong factors in her succumbing to tuberculosis.

Although there was general agreement that the patient's dyspnea did not justify surgical intervention, it was decided to perform prophylactic decortication in the event of a lung infection in the future. A stormy postoperative course was complicated by a depressive

reaction severe enough to require further psychiatric consultation and treatment.

In attempting to evaluate this case, the staff on the chest service first faced the task of correlating the marked respiratory symptoms with objective findings. Exhaustive respiratory studies failed to reveal a correlation, but the admission history disclosed evidence of psychopathologic disturbance—alcoholism. Further inquiry revealed phobias, severe anxiety states, inability to express anger directly, sexual frigidity, and unhappy marriages in which she was called on to support each husband.

The tuberculous infection with subsequent empyema and shortness of breath was associated with a decrease in anxiety. Despite organic improvement, dyspnea persisted. Thus, pre-existing unconscious conflict with extreme anxiety found relief in a symptom of organic causation. This was considered an example of one type of somatic compliance in the development of a conversion reaction. Undoubtedly another factor in the choice of this symptom was her experience in childhood when she found considerable gratification in the attention she received when seriously ill with diphtheria, an illness frequently associated with shortness of breath.

Case 2—A 21 year old man of Spanish-American descent came to the emergency room complaining of burning pain in the feet, aching pain in the legs, generalized weakness, and inability to walk. For the past six months there had been increasing slowness, clumsiness and difficulty in walking, which hampered his work as a gas station attendant. The flexors and extensors of the forearms and legs were weak. He was unable to sit without support, and there was loss of pain, touch, position and vibratory sensations just below the knees. Reflexes were normal.

The patient was admitted to the neurologic service, and the next day a neurologic examination was repeated. Position and vibratory sensations had returned, the sensory level for pain and touch differed from that found the previous day, and all muscle groups were strong.

During psychiatric interviews the patient disclosed that he was married in May 1956 and that his 17 year old wife was pregnant at the time. He also reported being married previously to a woman who "slept" with his father. He was unemployed at the time of his second marriage, and a few days before the birth of the baby in January 1957 his feet were frostbitten while he was looking for work. He was hospitalized, and careful examination failed to show evidence of peripheral vascular disease. He was overly concerned and suspicious about the medical care of his wife and child at the time of delivery. During the next six months he was unable to hold a job longer than 10 or 12 weeks and complained of swelling and of burning pains in his feet. He felt that fellow workmen did not like him, "rode" him, and blamed him for things because he was Spanish-American. He emphasized that his bosses liked him though they had to fire him.

In July 1957 his wife told him she was pregnant again. That night he had his first falling episode. His legs collapsed under him while he was carrying his young daughter. He worried a great deal about the problems another child would present. He fell several more times and was fired from his job when he walked off after a fight with his brother, who worked at the same place. The morning after this incident he was unable to walk. He spent the next 10 days trying to get around on crutches and on some homemade parallel bars. His wife insisted he go to the hospital, and threatened to leave him unless he did so.

The patient said he was suspicious of everyone, would not eat at his friends' homes, and thought there might be saltpeter in the hospital food. He always had a volatile temper and when he felt restless he would go out looking for a fight. Since his second marriage he had the impulse to strike his wife and child but felt he should not; he either walked out or flopped on the floor and became rigid.

The patient was the oldest of six children. During his childhood there was never enough food, and his mother drank and neglected the children. He was told that he did not walk until he was three and a half years old. His father, also an alcoholic, had tabes dorsalis and obtained from this hospital braces for

both legs so that he could walk. The patient had mixed feelings about his father. He said he hated him but also wanted to help him though his father had treated him brutally and told him he was a bum and never would amount to anything. The patient was extremely sensitive about being regarded as a "dirty Mexican" in his community.

When he was 17 years old he enlisted in the navy, where he stayed for two months. At that time he experienced a dissociative episode when he was about to be transferred from a backward company to one in which he could complete his training. Then he was discharged.

In the hospital the patient said he had "given up," that it did not matter if he walked again, and that he was better off in a wheel chair than walking around outside where "people ran you down and did not give you a break." He was desirous of obtaining braces to help him walk.

He did not show particular concern about his symptoms, and he alternated between being boyishly pleasant and threatening to leave the hospital in order to get his way. He remained, however, and seemed to enjoy his situation on the ward. Many times he had chest pain like that of some cardiac patients.

This case shows many of the characteristics of the hysterical character. The patient employed fantasy to the extent that his presentation of himself had little relation to what others observed in him and in the situations he described. There was a marked degree of exaggeration and distortion of cause and effect in his appraisal of events around him. He was egocentric and dramatic. He related only superficially and was suggestible in his acquisition of other patients' symptoms. His threats to leave the hospital, his frequent fights, and his liaison with a woman of his father's are examples of an inability to modify behavior by judgment.

His symptoms of inability to walk and of stocking anesthesia along with the history of a dissociative episode were typical of conversion symptoms and presented no problem in differential diagnosis. However, the pains in the feet and legs required evaluation to rule out peripheral vascular disease. No evidence of the latter was found, but the frostbite provided the locus of the somatic compliance on which his symptoms were elaborated. These began with painful feet and ended with inability to walk. The onset of the conversion reaction in its fullest form was sudden and under stress of his wife's second pregnancy.

Through his symptom he seemed to be identifying with his father, who had braces on his legs. Also, in his childhood he had frequently been displaced in his mother's affection by the arrival of younger siblings. He responded by forgetting or only slowly learning to walk. His marriage and competition with his children for his motherly wife recreated an earlier emotional situation with his mother, and he responded with the same functional disorder. This symptom partially gratified his wish for mother's affection. It also prevented him from expressing his destructive impulses against his child who, like his siblings, threatened to displace him in relation to his wife. He defended himself against this apparently unworthy wish by emphasizing his concern for the well-being of his child. However, he did not implement this concern by his ability to care or provide for his family.

The diagnosis of conversion reaction was easily made and was adequately supported by the typical character of his symptoms, the relatively clear symbolic meaning in the context of the precipitating circumstances, the presence of hysterical character traits, and, further, the fact that the anxiety about his wife's pregnancy was relieved with the onset of conversion symptoms.

Case 3—A 19 year old single man of Spanish-American descent entered the hospital the day he suddenly became blind. Ophthalmologic and neurologic examination was negative for organic impairment. He was a second-year student at a religious seminary, and on the day of admission he had been disturbed because of recent arguments with the director of discipline.

During his first year at the seminary the patient was admitted to a hospital at his own request and subsequently was diagnosed as having pneumonitis. On the third day in the hospital he experienced loss of voice, which

prolonged his stay an additional 10 days. After he returned to the seminary there were other episodes of loss of voice prior to the onset of blindness. From the patient's mother we gained the information that in high school the patient experienced "fainting spells" and loss of consciousness followed by headache on several occasions while playing football. These episodes seemed to occur when he was about to be blocked or tackled. Earlier in high school he had two "head injuries" while playing football. Medical and neurologic study at that time did not reveal organic disease. Aside from the episodes mentioned, there were no other illnesses requiring hospitalization.

When the patient was four years old his father was admitted to a state mental institution because of difficulties, according to the patient, resulting from a head injury. He is still hospitalized. The patient's mother divorced the father and remarried. He has two older brothers, aged 23 and 21 years, and four younger half-siblings. The mother reported that as a child the patient was scrupulously neat and clean and became greatly agitated and distressed when he was dirty. She further described him as a very observant, studious, retiring youngster, not as aggressive as his older brothers. In her opinion he was greatly influenced by his grandmother, with whom he had much contact. The grandmother was described as a rigid, strict person, particularly in religious matters, who possibly used subtle pressure to influence the boy in the direction of the priesthood.

The patient was a well-developed, well-nourished young man whom the nurses described as extremely polite. He was always neat and tidy in dress. His facial expression was for the most part fixed, and it was animated only when speaking of superficialities. In early interviews the emotional reaction was one of complacency, but later he reacted with anger at the interviewer whom he accused of being atheistic. He tended to provoke intellectual arguments. Large areas of amnesia concerning childhood events were noted, and vagueness about important dates. He related to the examiner in a superficially friendly and congenial manner. He reported that sexual thoughts were immediately banished from his mind to be replaced by prayers. It was obvious that he was markedly rigid in his codes of personal conduct, ethics and morality. As interviews progressed, obstinacy, anger and intellectualization became more prominent.

He readily admitted that blindness is a means of not "seeing" and therefore of excluding from the mind certain unacceptable thoughts. These were concerned with "blood, suffering and injury" and some undisclosed sexual fantasies. It was apparent that the anxiety associated with his sadistic and erotic preoccupations was bound by his hysterical blindness. Hence, his inappropriate blandness and complacency in spite of his "blindness" were understandable.

It is of considerable interest that he recovered rapidly following the discussion relating his blindness to unacceptable fantasies.

Summary

The main differential points in distinguishing between conversion reaction and organic disease are presented, with emphasis on the lack of anxiety, the sudden and dramatic onset, and the distortion of a particular function (rather than an anatomic entity) as important features of conversion reactions. Psychiatric disorders requiring differentiation from conversion reactions are described: secondary gain from symptoms, psychosomatic disorders, hypochondriasis and malingering.

Symptoms of conversion reaction are described and discussed. They tend to take on certain forms but can directly or indirectly involve any organ or tissue and may simulate every known functional disturbance. The choice of symptom is discussed with reference to the psychologic meaning of the symptom. It is described how anxiety is relieved by the conversion symptom. A hysterical character disorder is the personality type in which conversion symptoms are most often observed.

To illustrate the diagnostic features, three case reports are presented: a case of dyspnea in a woman with tuberculosis, a case of motor and sensory changes in a man who previously had frostbite, and a case of blindness in a patient with a history of head injuries.

Trends in Chemotherapy of Cancer

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RECENT statistics estimate that about 24 million or one of every seven persons in the United States will die of cancer unless new methods of treatment or prevention are found. This article considers some of the recent developments in the field of chemotherapy of cancer.

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Today our chief measures for control of cancer are surgery and radiation therapy. We can cure many cancers if the diagnosis is made when the disease is confined to the site of origin. With the many improvements in surgical technic and postoperative care, complete removal of a malignancy is safer and more effective. Better radiation therapy has resulted from advances in high-voltage engineering, nuclear research and radiobiology. In addition, nuclear research has extended the scope of radiation therapy considerably by providing a number of radioisotopes (Co^{60}, P^{32}, Au^{198}, I^{131}). With a combination of technics the surgeon and radiologist can cure many cases of cancer. Unfortunately even with the best of present-day therapy only about one-third of patients with malignancy survive five years after the diagnosis is made. This is due in large part to the invasive nature of many cancers which disseminate widely before the primary tumor is discovered.

The hope of finding a selective agent for the treatment of metastatic cancer has long inspired research in the field of chemotherapy. Significant advances have rewarded the research efforts of the past 10 years, and today the temporary control of some forms of cancer with chemical agents is a reality. Many recent discoveries and improved technics promise even greater success for the future. I have selected for discussion several areas of research which seem to be highly promising or give a new or different approach to the complex problem of treatment of cancer. This arti-

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cle is in no sense a review, but is one in which I have taken the privilege of selecting the topics for discussion. The reader is referred to several excellent reviews[1-4] of the subject for many details not here considered.

Many significant advances in chemotherapy of cancer are attributable to improved technics. In recent years cooperative groups whose staffs include full-time scientists with special training (cytologists, biochemists, pharmacologists, clinicians) have largely replaced the individual investigator in cancer research. While the latter continues to make important contributions, cancer research is becoming a collaborative endeavor with full-time staffs of scientists and clinicians working toward a common goal.

Recognition by the government, the public and the medical profession of the value of collaborative research in the field of cancer has led to the establishment of many agencies whose specific purpose is the study of cancer in its various aspects. Among such groups are The Children's Cancer Research Foundation of Harvard Medical School, Sloan-Kettering Institute for Cancer Research, Southern Cancer Research Institute, Roswell Park Memorial Institute, and many others.

A further step in the direction of collaborative research is the establishment of the Cancer Chemotherapy National Committee. A committee of the National Advisory Cancer Council has joined with the American Cancer Society, the Damon Runyon Foundation, the Veterans Administration, the Atomic Energy Commission, and the Food and Drug Administration to form the Cancer Chemotherapy National Committee, which in cooperation with the pharmaceutical industry has established a voluntary cooperative program. A Cancer Chemotherapy National Service Center has been created at the National Cancer Institute. Cooperation with institutions in other parts of the world has been arranged. Four large panels concerned respectively with organic chemistry, screening, pharmacology and biochemistry, and clinical investigation are speeding progress in these various areas. This voluntary program is providing help, funds and information to the cancer chemotherapy program in an organized manner and on a scale never before attempted. Such an agency can be of inestimable value in the all-out effort to conquer cancer.

Many if not most of the carcinolytic drugs in clinical use today were discovered through empirical studies—by observing their effect on tumors in animals, their growth-inhibiting effect on cells grown in tissue culture, their effect on bacterial growth, and so forth. After the initial observation indicating growth inhibition, studies must be undertaken to establish the safe maximal dose and the pathologic changes in the tissues before the drug may be tried clinically. One of the services provided by the Cancer Chemotherapy National Service Center is the screening of compounds for possible anticancer activity. During 1956 more than 12,000 compounds were obtained for testing against cancer in animals, principally mice. It was anticipated that the number of compounds submitted in 1957 would exceed 35,000. The compounds sent for testing are primarily synthetic organic chemicals and filtrates obtained from microorganisms. In the process of screening it is considered necessary to test each compound against at least three different types of tumor in inbred mice. Up to 10 mice may be required for a single test. It was estimated that a million inbred mice would be needed to carry out 100,000 tests during 1957.

Many other biologic tests besides those conducted on cancer-bearing animals are being employed to assess the chemotherapeutic agents. Comparative studies have been carried out to determine the cytotoxic action of various compounds against established cell lines of normal human tissue (adult liver) and malignant human carcinoma (epidermoid) grown on synthetic media containing dialyzed human or horse serum. Eagle and co-workers used this technic in a study of more than 200 drugs having growth-inhibitory action. Tissue culture methods such as this permit more quantitative studies than do those on animals and are less expensive. A further important advance is the development by Puck and Marcus of a system for growing clones from single human cells. This technic will be invaluable to

geneticists and biochemists and to those doing research in cancer chemotherapy.

Another method of testing cancer-inhibitory drugs employs rats or hamsters which have been exposed to x-ray or given cortisone, or both. Toolan of Sloan-Kettering Institute transplanted and maintained many human tumors in such animals. This method affords a means of studying the response of tumors of human origin to drugs, antibiotics, antibodies, and so on. It has been established that the transplanted tumors retain their human genetic properties.

After a compound is discovered to have carcinolytic properties by studies on animals bearing malignant tumors or by other means, and pharmacologic studies have established its toxicity and safe maximal dose, its effectiveness in human cancer must be evaluated. This is an expensive, time-consuming process requiring special attention to methodology. Even the large research centers can carry out such a study on only a few patients over a period of many months. To overcome this difficulty a number of clinical investigators have formed cooperative research groups of 5 to 10 persons from several institutions. A group draws up a joint protocol which each investigator uses, so that the same types of cancer are treated with the same compounds in exactly the same way. This provides a means for comparing the effectiveness of various compounds and the results on a large number of patients from several institutions.

The clinical cancer chemotherapist is beset with certain problems which make controlled studies difficult. The drug must always be used as part of the total care of the patient. It is, of course, inexcusable to include untreated controls as does the investigator who uses animals. Further, the coexistence of many other disorders such as hypertension, renal disease and liver disease may influence the results and must be taken into account. Finally the clinician faces the problem of assessing the effects on tumor growth. This requires extensive clinical and laboratory examinations such as hematologic and bone marrow studies and photography and x-ray examination at frequent intervals. Other laboratory tests on blood, excreta and body fluids, tests of liver or kidney function, and certain enzyme studies all are part of the well-conducted experiment. Tumor masses should be measured with calipers, and histologic examination of the tumor and its exact classification are necessary. Final evaluation must be based on the effect on the growth of the primary tumor or metastases as well as marked improvement in the patient's health and prolongation of life.

The list of compounds which have a place in treatment of one or another form of disseminated neoplastic disease is a long one and includes such accepted remedies as ACTH, cortisone, estrogens, prednisone, androgens, urethan, triethylene thiophosphoramide (thio-TEPA), triethylene phosphoramide (TEPA), triethylene melamine (TEM), nitrogen mustards, MYLERAN® (busulfan), chlorambucil, AMINOPTERIN®, amethopterin (Methotrexate) and 6-mercaptopurine. Each of these agents has produced palliation or prolonged remission in some type of cancer. Unfortunately the cancer sooner or later becomes resistant, and we must admit that no presently available carcinolytic agent can cure neoplastic disease.

The fact that resistance ultimately develops to all the presently known cancericidal agents has stimulated research workers to discover other and better drugs. Drug resistance itself is the subject of much research employing modern chemical technics.

Attempts to develop better carcinolytic agents have been materially aided by progress in related fields. Studies of the metabolism of various types of cancer cells have given important leads which are being vigorously explored. The mechanisms of carcinogenesis are being actively studied by modern biochemical methods, and these efforts have uncovered interesting leads. Perhaps the most important developments have come from investigation of the structure and metabolism of the nucleic acids and their relationship to genetics. The following discussion is in part an excerpt from an article by Hamilton:[5]

"It has long been known as a result of classical studies in cytology and genetics that the chromosomes contain the genes which determine the character and rate of growth of

cells. Chromosomes contain protein, desoxyribose nucleic acid (DNA) and a little ribose nucleic acid (RNA). The evidence is good that DNA is the substance of the gene responsible for the specificity of the hereditary material.

"It has been shown that the hereditary character of bacteria can be changed by treatment with DNA extracted from another strain of the same species. Numerous other studies with bacteriophages also point to DNA as the hereditary material. Other extensive investigations both chemical and employing x-ray diffraction analysis have allowed the construction of three-dimensional models of DNA. Such lines of investigation have shown among other things that the basic structure or skeleton of DNA is the same in all cells. This appears to be true in both the cancer and normal cells."

The question arises, What is responsible for the specificity of DNA?

"The most obvious chemical differences in DNAs from different species arise from variations in the amount of the nitrogenous constituents, the purines and pyrimidines. From studies on the DNA composition of nearly 50 species it has been shown that the amounts of adenine and thymine are about equal, and similarly the amounts of guanine and cytosine are also about equal. However, the ratios of adenine to guanine and of thymine to cytosine vary considerably in different species. Further considerations have led to the belief that the arrangement of these nitrogenous building blocks in the DNA molecule is the basis for the specificities of DNA and for their exact replication in genetic processes. Since it appears that cancer cells develop as a result of modifications of the genetic makeup of normal cells it may eventually be possible to establish the specific chemical differences in the DNA of cancer cells.

"Studies of DNA synthesis by different cells have revealed qualitative or large quantitative differences in nucleic acid metabolism. For example there is a considerable diversity in the patterns of purine utilization in nucleic acid synthesis. Chemotherapeutic studies seek to exploit these differences by introducing analogues which would interfere with these anabolic processes in the synthesis of DNA."

Investigations founded on the scientific structure just described bid fair to provide a new basis for rational cancer chemotherapy. In fact, much research is under way using possible antimetabolites of adenine, guanine, thymine or cytosine. Recent studies have employed several antimetabolites of the purines and pyrimidines (6-mercaptopurine, 6-chloropurine, 6-azauracil, 5-fluororotic acid, 5-fluorouracil, etc.) as tumor-growth inhibitors in animals; some of the compounds are undergoing clinical trial.

Many recent advances in chemotherapy of cancer are based on previous studies and represent improvements of agents previously in use. In succeeding paragraphs I shall consider certain of these newer drugs, as they appear to represent real progress.

The various chemotherapeutic cancericidal agents have been classed as follows:

1. Polyfunctional cytotoxic agents.
2. Antimetabolites.
3. Hormones.
4. Antibiotics—bacterial and plant metabolites.
5. Oncolytic viruses.
6. Miscellaneous substances (urethan, arsenic, antigens, guinea pig serum, etc.).

Only some of the recent advances under each of these classes will be discussed. Details will be found in the reviews mentioned previously[1-4] and in the more recent literature.

Polyfunctional Cytotoxic Agents

The original representative and prototype of the polyfunctional cytotoxic group is nitrogen mustard, the discovery of which was a useful by-product of studies on war gases during World War II. Nitrogen mustard (mechlorethamine) has been widely used and found useful in Hodgkin's disease, certain forms of lymphosarcoma, chronic leukemia and bronchogenic carcinoma. It is classed as an alkylating agent in that it introduces alkyl groups in place of hydrogen into many organic molecules. Its two ethyleneimine groups are the basis for its toxicologic and tumor-inhibiting activity. It is particularly injurious to cells

that divide rapidly, both normal and neoplastic. Biochemical and cytologic evidence implicating the chromosome, a complex nucleoprotein, as the cellular target of compounds of this type is increasing. It may be significant that in vitro and in vivo experiments have established that the nitrogen mustards and other alkylating agents react readily with nucleoproteins and nucleic acids.

Many other members of the polyfunctional cytotoxic group have had fairly wide clinical trial. Triethylene melamine (TEM), triethylene phosphoramide (TEPA) and triethylene thiophosphoramide (thioTEPA) are among those having cancericidal action and possessing certain advantages over nitrogen mustard itself, such as oral use, less local and systemic toxicity, and somewhat greater selectivity of action.

Two new members of this group, busulfan (Myleran) and chlorambucil (leukeran) appear to have a definite though limited place in chemotherapy of cancer. Myleran is a sulfonic acid ester similar in action to the other polyfunctional alkylating agents. It appears to be more selective than nitrogen mustard or the folic-acid antagonists in its effect on myeloid cells, and may also be somewhat safer. When properly used it depresses myelopoiesis with little effect on lymphocytes and platelets. Larger doses, however, depress the platelet count and cause hemorrhages. The drug may depress the bone marrow irreversibly, and this may not be evident for four to six months. Blood counts at weekly intervals are mandatory in patients receiving this drug, and it must be stopped or the dose reduced at the first sign of bone marrow depression. Busulfan has proved of value in chronic myelocytic leukemia. It is not curative but it may effectively control symptoms. It has been especially useful in patients who no longer respond to radiation therapy or other chemotherapeutic agents.

Chlorambucil, a derivative of nitrogen mustard, has been recommended in treatment of chronic lymphocytic leukemia, malignant lymphomas (including lymphosarcoma), giant follicular lymphoma and Hodgkin's disease. It is not curative but may produce striking remissions. It is easier to handle than nitrogen mustard because it produces fewer side effects and is not as depressing to the bone marrow. As with busulfan, it is necessary to follow the blood count carefully in patients receiving chlorambucil. Blood counts should be taken once or twice weekly, and the dosage should be reduced or the drug discontinued when there is evidence of abnormal depression of the bone marrow.

Many other polyfunctional cytotoxic agents are under investigation but none have been studied clinically in sufficient detail to warrant discussion here.

Antimetabolites

Folic-acid antagonists—These drugs have been the most widely used antimetabolites, and perhaps this is why their action is better understood. Of the several compounds that have been synthesized, Aminopterin and Methotrexate (amethopterin) have been especially useful in acute leukemias in children. Good clinical and hematologic remissions have been obtained in 30 to 50 per cent of cases. They are less effective in acute leukemia in adults, but may induce remissions. It may take as long as eight weeks to obtain a remission. The remissions average eight months in duration (from one month to two years).

Purine antagonists—Purine antagonists are another type of antimetabolite introduced recently. They have been useful in leukemia. The compound that has had the most extensive trial is 6-mercaptopurine. It is given orally in a dose of 2.5 mg. per kilogram of body weight daily. From 3 to 12 weeks of treatment may be required to induce a remission. Approximately one-third of the children with acute leukemia and one-seventh of the adults to whom 6-mercaptopurine has been given have had remissions. The compound has also produced good responses in most of the early cases of chronic granulocytic leukemia in which it has been tried.

Several other antipurines, including thioguanine and 6-chloropurine, have had limited trial but their exact position as cancer chemotherapeutic agents has not been established.

Pyrimidine antagonists—Several antagonists of pyrimidine have been under investiga-

tion recently but they have not had extensive clinical trial. Welch, Shnider and co-workers reported that 6-azauracil exerts a competitive antagonism to uracil in certain bacterial strains and that it shows moderate antitumor activity against several strains of transplantable tumors in animals. Mice, cats, dogs and monkeys tolerated the drug well. However, when it was tested on cancer patients, toxic manifestations mainly referable to the central nervous system were encountered. These included somnolence, disorientation, hallucinations, hyperreflexia, mental retardation and incontinence. Children appeared to be more susceptible than adults. It would seem that toxic effects on the central nervous system will seriously limit the use of this antimetabolite as a carcinolytic agent.

Another new series of pyrimidine analogues have been developed by Heidelberger and associates. These are 5-fluorouracil and related compounds. It was found that 5-fluorouracil exerted tumor-inhibitory activity against a variety of transplantable tumors in rats and mice. McIver and associates are conducting a clinical trial of the drug on a group of far-advanced cases of malignant disease. Their results will be awaited with interest.

Nicotinamide antagonists—Thiodiazoline was synthesized in 1954 and was found to inhibit mouse leukemia. Clinical trial in several institutions failed to produce a favorable therapeutic response. However, toxicity of some degree was noted in all patients. Other nicotinamide antagonists are under investigation.

Hormones

It has been shown that many cancers are not autonomous but are dependent on hormonal support. The observation that certain tumors in tissues controlled by the sex hormones may be under hormonal control has led to several successful measures for modifying tumor growth. Large doses of androgenic, estrogenic and adrenocortical hormones often are effective in treatment of carcinoma of the breast and of the prostate. Adrenocortical hormones have been useful in the lymphomas and leukemias as well as in certain cases of carcinoma of the breast and of the lung. Many recent studies have been devoted to a search for more active steroid analogues with more prolonged action and fewer side effects. Other investigations have explored fundamental mechanisms. The reader is referred to a recent symposium sponsored by the American Cancer Society entitled "Role of hormones in the origin and control of abnormal and neoplastic growth"[6] for a detailed discussion.

Antibiotics

Stylomycin (puromycin), an antibiotic isolated from *Streptomyces alboniger*, has shown activity against experimental tumors. Clinical trials with it have been rather disappointing.

Another antibiotic, azaserine, derived from a species of *Streptomyces*, has exerted antitumor action against sarcoma 180 and various strains of mouse leukemia. It was found to act synergistically with 6-mercaptopurine against sarcoma 180 and some strains of mouse leukemia, and suggestive evidence of this synergism was found in children with acute leukemia. A cooperative clinical investigation sponsored by the Clinical Panel of the Cancer Chemotherapy National Committee is under way to determine the extent of this additive effect.

Several other antibiotics from various species of *Streptomyces* have been under investigation since 1949. Actinomycin C has had considerable clinical trial in France and Germany. Hodgkin's disease and other lymphomas have been benefited especially in the early stages. Effect of the drug on other tumors was not remarkable. A combination of irradiation and actinomycin C may be more effective than either agent alone.

A related antibiotic, actinomycin D, was found to have a high degree of carcinolytic action against transplantable mouse tumors. Limited clinical trials with actinomycin D show some degree of anticancer effect but the drug is highly toxic and tolerance develops readily.

Oncolytic Viruses

Viruses often show a predilection for certain organs or tissues such as lung, central nervous system and liver. Certain neurotropic viruses have been shown to grow in tumor

cells and cause their destruction. Investigators recently have attempted to develop a virus or viruses with tumor specificity by growing them in tissue cultures of tumors or in tumor-bearing animals. Several neurotropic viruses originally obtained from Africa destroy human cancer cells grown in tissue culture, in embryonated eggs, and in rats. Some of these viruses show promise of clinical application. A recent report by Kato and associates indicates that the pox group of viruses (ectromelia, vaccinia, fowlpox and psittacosis) have a remarkable affinity for cancerous cells. Tests were made on ascites tumors (Ehrlich and Yoshida), S-37 and Rous chicken sarcoma. Results of further studies along these lines will be awaited with interest.

Immunologic Studies

Some scientists are employing immunologic principles in cancer chemotherapy. The observation that tumors sometimes regress spontaneously and the possibility that the body may possess some natural defense in the early stages of cancer provide some justification for this approach. There is some evidence that man is capable of forming antibodies against certain tumors. Other studies are exploring the possible use of auto-immunization or heterologous antiserums in treatment. Recently a group at Sloan-Kettering Institute demonstrated that zymosan, a yeast product, in low dosage exerted a remarkable antitumor effect against sarcoma 180, a mouse-transplantable tumor. It is believed that the small doses of zymosan stimulate production of properidin by the body.

Studies more directly related to human cancer seem to indicate that properidin may be concerned in some way with cancer immunity. Persons who have cancer have a lower than normal level of properidin in the blood, and cancer transplants are accepted readily; normal persons who have higher properidin levels are much more resistant to the transplantation of cancer cells.

Combination Therapy

Numerous clinical and experimental studies indicate that the chemotherapeutic agents can be combined to advantage with surgical or radiation therapy. Under certain conditions the anticancer drugs themselves may be combined to advantage.

Recent work suggests that certain chemicals may potentiate the effect of x-rays remarkably. The combination of a new chemotherapeutic agent, 6-aminonicotinamide (6AN), an antagonist of nicotinamide, and radiation raised the cure ratio from transplanted cancer of the breast in mice to 86 per cent. Radiation alone cured 27 per cent. Similar results have been obtained with the combination of 6-mercaptopurine and radiation. Bane, Conrad and Tarnowski[7] recently reviewed the subject of combination therapy. Their article gives many other examples of the synergistic action of chemicals and radiation.

Chemoprophylaxis as an aid to surgery is a recent application of chemotherapy in cancer.[8] We have long known that despite a thorough operation a cancer may recur in one or two years with widespread metastases. There has been a growing suspicion that a few cancer cells left at operation disseminate soon afterward to give rise to widespread neoplastic disease. Warren H. Cole, working on the hypothesis that exfoliated cells at operation could be responsible for dissemination, observed in operations on animals simulating the surgical removal of human tumors that cells escape and bring about recurrence of the cancer. Observations by other surgeons and pathologists point to a substantial spread of cancer cells at operation.

Cole and associates studied the possibility of chemoprophylaxis against this widespread dissemination. They injected 110,000 to 220,000 cancer cells into the portal veins of rats. Half the animals were treated with various dosages of nitrogen mustard, thioTEPA and other anticancer drugs. The other animals were untreated. In one series, cancer developed in 7.1, 17.8 and 16.2 per cent of the treated animals, and in 90, 92.1 and 92.3 per cent of the untreated controls. It was necessary to inject the drugs soon after inoculation with cancer cells; drugs given 48 hours after inoculation produced no effect.

Long-term studies were then begun on pa-

tients. "Every other patient with cancer of the breast, rectum, colon or stomach is given prophylactic treatment. These four sites were selected because they are drained by veins as well as lymphatics. The following routine is now used in test patients: (1) All vessels serving the operative site are tied off. (2) At the end of the operation a drug is given intraperitoneally to kill stray cancer cells. (3) On each of three days following surgery the patient is given the drug intravenously." The results of these well-controlled studies will be of great interest.

It is apparent that research in the field of cancer chemotherapy, both experimental and clinical, is being better planned and better coordinated. Knowledge of cellular growth and metabolism gained through newer technics of fundamental biology and biochemistry is being applied in a rational manner to the development of newer drugs. The related and highly important fundamental problems of why cells become malignant and why they develop resistance to the presently available chemotherapeutic agents are under investigation. It seems not impossible that one or another of these approaches may provide the answer to the control of metastatic cancer.

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Books Received

Books received are acknowledged, and, as space permits, those of principal interest to our readers are reviewed more extensively. Reviews appear in this issue starting on page A-128; additional listings are on pages 173 and A-144.

Understanding Your Patient. Edited by Samuel Liebman, M.D., Medical Director, North Shore Hospital, Winnetka, Illinois, with 10 contributors. 170 pages. 1957, J. B. Lippincott Company, Philadelphia and Montreal. $5.00.

Advances in Radiobiology; Proceedings of the Fifth International Conference on Radiobiology held in Stockholm on August 15 to 19, 1956. Edited by George Carl de Hevesy, Arne Gunnar Forssberg and John D. Abbatt. 503 pages, illustrated. 1957, Charles C Thomas, Springfield, Illinois. $15.50.

The Relation of Psychiatry to Pharmacology. By Abraham Wikler, M.D., National Institute of Mental Health Addiction Research Center, Bethesda. Published for the American Society for Pharmacology and Experimental Therapeutics. 322 pages. 1957, The Williams & Wilkins Company, Baltimore. $4.00.

Cerebral Lipidoses; a Symposium. By L. van Bogaert, M.D., Director, Department of Neurology and Neuropathology, Institute Bunge, J. N. Cumings, M.D., Clinical Pathologist, The National Hospital, London, England, and A. Lowenthal, M.D., Department of Neurology and Neurochemical Research, Institute Bunge, Antwerp, Belgium. 212 pages, illustrated. 1957, Charles C Thomas, Springfield, Illinois. $8.50.

Cardiovascular Rehabilitation. Edited by Paul Dudley White, M.D., Massachusetts General Hospital, Boston; Howard A. Rusk, M.D., Director, Institute of Physical Medicine and Rehabilitation, New York University-Bellevue Medical Center, New York; Bryan Williams, M.D., Clinical Instructor in Medicine, Southwestern Medical School, University of Texas, Dallas, and Philip R. Lee, M.D., Department of Internal Medicine, Palo Alto Clinic, Palo Alto, California. 155 pages. 1957, The Blakiston Division, McGraw-Hill Book Company, Inc., New York, Toronto and London. $6.50.

Year Book of Pediatrics; 1957-1958 Year Book Series. Edited by Sydney S. Gellis, M.D., Professor of Pediatrics and Chairman of the Department of Pediatrics, Boston University School of Medicine, Boston. 469 pages with 153 illustrations. 1957, The Year Book Publishers, Inc., Chicago. $7.50.

Pre-Employment Disability Evaluation. By William A. Kellogg, M.D., formerly associated with the Medical Department, Douglas Aircraft Company, Inc., Long Beach, California, and Clinical Professor of Surgery, New York Polyclinic Post-Graduate Medical School, New York. 155 pages. 1957, Charles C Thomas, Springfield, Illinois. $10.50.

Introduction to Anesthesia; the Principles of Safe Practice. By Robert D. Dripps, M.D., Professor and Chairman, Department of Anesthesiology, James E. Eckenhoff, M.D., Professor of Anesthesiology, University of Pennsylvania, Philadelphia, and LeRoy D. Vandam, M.D., Clinical Professor of Anesthesia, Harvard Medical School, Boston. 266 pages. 1957, W. B. Saunders Company, Philadelphia and London. $4.75.

Diffuse Obstructive Pulmonary Emphysema, a Poorly Understood Disorder

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THE diagnosis of emphysema† is frequently applied to disorders that are in reality other forms of cardiopulmonary disease. Conversely emphysema is often overlooked as a cause of cardiac decompensation. Wide disagreement among clinicians on the diagnosis is matched by disagreements among radiologists, pathologists and even pulmonary physiologists.[1-9]

Christie and Knott[10] found that a group of radiologists were 75 per cent correct in diagnosing emphysema and 80 per cent correct in interpreting normal roentgenograms when they read the posteroanterior and lateral inspiratory and expiratory chest films of a test group of subjects. When they read only inspiratory posteroanterior films they were 75 per cent correct in diagnosing emphysema and only 40 per cent correct in interpreting the normal roentgenograms. Monroe[11] reviewed all the medical admissions of persons more than 61 years of age who came to necropsy at the Peter Bent Brigham Hospital in Boston from 1913 to 1943 and found a positive correlation between the clinical diagnosis of emphysema and the pathologic report of the disorder in only 4 per cent. Not only was emphysema sometimes found pathologically when it had been unsuspected clinically; often the condition was not found post mortem when it had been diagnosed during life.

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†The term emphysema as used in this paper refers to the generalized disease.

Definition

Diffuse obstructive pulmonary emphysema is a chronic, usually progressive idiopathic disorder of the lungs characterized by the following findings:

Pathologic—Shallow, widened alveoli with thin, often ruptured walls; bullae; some fibrosis; occasional pneumothorax; frequent chronic cor pulmonale; no demonstrable evidence of obstruction of the airway.[5, 12-16]

Physiologic—Striking reduction in maximal breathing capacity; absolute and relative increases in residual volume; impaired mixing of gases;[17] retention of carbon dioxide;[1] increased respiratory work on hyperventilation;[18] increased gradient of the pressure necessary to transfer the oxygen across the pulmonary membrane.[3, 8]

Radiologic—A large, bright lung field in both posteroanterior and lateral views; increased retrosternal and retrocardiac spaces; kyphosis; occasional bullae; a low, flattened, relatively immobile diaphragm; slow filling and very slow emptying by fluoroscopy; occasional enlargement of the heart, especially the right ventricle and atrium.[10, 19]

Clinical—Dyspnea unexplained by other findings; difficulty in moving air in and especially out of the lungs; frequent ultimate complication of right-sided heart-failure; poor correlation with the pathologic, physiologic and radiologic findings.[9]

Etiology

The cause of emphysema remains obscure.[5] To discerning clinicians and pulmonary physiologists there is little doubt that there is obstruction to air flow, particularly on expiration and most notably on forced expiration. Pathologists have so far been unable to identify the obstruction.[20, 21] The fact that the obstruction cannot be seen leads one to surmise that it is either somewhere in the finer respiratory passages or caused by partial or complete collapse of small cartilage-containing bronchi during expiration. The latter possibility is supported by the fact that the major bronchi and trachea have been observed bronchoscopically to collapse partially during forced expiration.

Another possible cause of functional expiratory obstruction of the bronchioles is paralysis of ciliary action.[22] This might result from inhalation of industrial gases or other noxious substances such as tobacco smoke.[23] The concept of paralysis of ciliary action receives some support from the observation that among inhabitants of the smog-ridden industrial cities of Great Britain emphysema invariably follows a long history of chronic bronchitis.[5, 6] In fact, it is postulated, especially in Great Britain, that recurrent and chronic bronchitis is a definite infectious disease entity and that it is the cause of most cases of emphysema.

Since emphysema often follows a long history of bronchial asthma and since it behaves superficially quite like nonepisodic asthma, some observers suggest that the disorder may arise from bronchospasm. Other workers propose, on the basis of the marked alteration in pulmonary vasculature with high pulmonary artery pressure, reduced pulmonary blood flow, and apparent hypertrophy of the bronchial vascular system, that changes in the bronchial circulation may be primary rather than secondary.[24] The enlargement of the thorax, especially in the posteroanterior diameter, the high clavicles, the widened rib spaces, and the kyphosis seen so frequently, especially late in the disease, have given rise to the hypothesis that there is some primary skeletal disorder. Heredity and impaired nutrition also have been considered as possible etiologic factors. In certain cases an occupational origin is still seriously entertained.[25, 26]

Degeneration, atrophy or accelerated aging is perhaps the basis of the most widely held hypothesis.[7] The universal finding that pure obstructive emphysema is almost limited to males must have some etiologic significance. It may well be that multiple factors, including loss of elasticity[27, 28] from the stress of chronic cough, chronic infection, chronic inflation from obstruction, and low resistance to wear and tear from accelerated aging, all play prominent roles.[5]

Other Forms of So-called Emphysema

This report does not concern various special types of emphysema.[6] *Localized bullous*

emphysema may be congenital or possibly acquired as a result of infection,[29] and may be relieved by surgical excision[30-32] or act as a common cause of spontaneous pneumothorax. *Senile or atrophic emphysema* is indistinguishable from the disease under discussion except that it comes on late in life and seldom causes severe disability, and bronchial obstruction usually is relatively mild.[7] *Kyphoscoliotic emphysema* gives an accelerated, almost malignant picture of true emphysema, and why it does not occur in all cases of kyphoscoliosis is not known. The fact that a study of this syndrome has not given us a better understanding of true emphysema has been disappointing. It presents an interesting argument for the hypothesis that the conventional type has a structural etiology. *Compensatory emphysema* is a misnomer. The term is sometimes applied to overdistended lung. There is no clear evidence that overdistention of lung per se has any causative significance in emphysema, although it may aggravate the condition. *Acute vesicular or interstitial emphysema* is a complication of severe respiratory infection, especially in children, characterized by the escape of air into the pulmonary parenchyma. Like *mediastinal emphysema*, in which air escapes into the mediastinal tissues, it has no connection with the disease under discussion. *Subcutaneous emphysema* is a misleading term applied to the escape of air into the subcutaneous tissues.

Clinical Picture, Course and Prognosis

Clinical picture—Patients who have emphysema complain chiefly of dyspnea on exertion, usually with fatigability. The onset often is gradual after many years of chronic cough, but it may be quite abrupt with no history of cough. The patients may relate a history of frequent respiratory infections with episodic dyspnea quite suggestive of bronchial asthma. Rarely there is no appreciable disability until right-sided heart-failure becomes apparent with dilated neck veins, gross enlargement of the liver, dependent edema, and dyspnea. Patients who have pure emphysema, with or without right-sided heart-failure, are not often orthopneic. Many who seem to breathe more easily when leaning forward report that they often are as comfortable lying flat as sitting forward. In late stages of the disease, cyanosis, polycythemia and clubbed fingers are common findings. Striking loss of weight occurs in almost all instances as the dyspnea becomes disabling.

The following clinical classification of dyspnea has proved useful:

CLINICAL DYSPNEA INDEX

0—No dyspnea; breathing equal to that of other persons of same age, sex and build, while walking or climbing.

+—Some difficulty climbing, but patient can walk a mile at own speed.

++—Patient can climb one flight of stairs or walk 100 yd. on level without stopping, but no more.

+++—Patient is less able to climb stairs or walk distances but does not have dyspnea at rest.

++++—Dyspnea at rest.

In the early case of emphysema there are no outstanding physical abnormalities at rest, and dyspnea is evident only on exercise. In advanced emphysema there is obvious respiratory distress even at rest and the patient is underweight. The most reliable physical findings in the chest are the signs of impaired ventilation: (1) impaired breath sounds with prolongation of the expiratory phase, and (2) inability to increase the intensity of the respiratory murmur to any great degree. Physical findings in the chest of secondary importance are (3) hyperresonance, (4) impaired cardiac and liver dullness, (5) limitation of thoracic and especially diaphragmatic motion, (6) chest movement "en bloc," (7) use of accessory muscles of respiration, (8) kyphosis and (9) high clavicles.[33] Unreliable signs of emphysema are barrel chest and a widened subcostal angle.

Roentgenography—The unreliability of the simple posteroanterior roentgenogram of the chest already has been stressed. Paucity of vascular markings is said to be a feature of early emphysema, but when the pressure in the pulmonary artery begins to rise and, more particularly, when right-sided heart-failure appears, the vascular markings often are in-

creased, especially at the hila. Lateral films often will show an increased posteroanterior diameter of the thorax with a resultant increase in the retrosternal space and some kyphosis. In advanced cases the diaphragm is flattened and the costophrenic angles are blunted. Bullae may be seen. Expiratory films will show reduced diaphragmatic movement when the disease is advanced, but this finding is reliable only when the patient is cooperative and the technician is well trained. In early cases diaphragmatic movement may be apparently normal or almost normal as measured on the inspiratory versus the expiratory film, especially if the patient is allowed time to empty his lungs fully.

Fluoroscopy—Fluoroscopic examination reveals a reduced degree of emptying of the lungs and especially a delayed *rate* of emptying, not always detectable on the inspiratory and expiratory films. In advanced emphysema various roentgenologic methods often will reveal enlargement of the right atrium, right ventricle and main pulmonary arteries.

Electrocardiography—An electrocardiogram may show right axis deviation and a prominent P_2. In later stages, right ventricular strain may be more evident, but unfortunately the electrocardiogram is quite insensitive as a guide to functional capacity of the right side of the heart and the lesser circulation.[34] Moderate to severe polycythemia is common.

Pulmonary function tests—We have already mentioned the pulmonary functional abnormalities seen in emphysema.[35-37] Pulmonary function tests are particularly helpful in cases of patients whose history is presumably unreliable or who have arterial hypertension or heart disease. Occasionally one will find an increase in the ratio of residual volume to total volume—i.e., more than 35 per cent—in the absence of emphysema. Rarely in true emphysema the only abnormality detectable by means of pulmonary function tests is a low maximal breathing capacity plus impaired mixing and diffusing capacities. A small amount of carbon dioxide in the inspired air may cause an abnormally small increase in minute ventilation in patients with emphysema. This is thought to indicate a selective depression of the respiratory center. Such a finding may prove to be a useful diagnostic or prognostic test.[38,39]

Emphysema is characterized functionally by an increase in respiratory work[18,40] (as measured by intra-esophageal or intrapleural pressures[41]), an increase that is abnormally rapid as activity is increased. This is due chiefly to increased airway resistance[42] and is regarded as one explanation for the extreme dyspnea so characteristic of the disease. In all probability, chronic hypoxia at least aggravates the pulmonary hypertension that is such a constant late feature.

Course—The course of emphysema varies widely.[3] In some cases deterioration progresses to a certain point and then levels off and apparently ceases. In others the condition follows a slow but inexorable downward course to terminal cerebral anoxia or chronic cor pulmonale and death.[34] It is noteworthy that some patients die of pure respiratory insufficiency—i.e., asphyxia—without evidence of cor pulmonale. At the other extreme, a few patients have right-sided heart-failure as an early or even a primary manifestation. In an important group of cases, a group that is quite small in Great Britain but much larger in the United States, the disease runs a malignant course of 18 to 36 months from the first symptom to death. The patients in this group usually are middle-aged men whose histories contain little if any evidence of antecedent bronchitis, and who often have *no history of cough*. Coexisting arteriosclerosis of the coronary vessels, arterial hypertension or other conditions leading to myocardial insufficiency may hasten cor pulmonale.

Complications—The complications of emphysema are chronic cor pulmonale, spontaneous pneumothorax and, rarely, failure of vision (papilledema resulting from increased venous or intracranial pressure[5]). Acute and chronic bronchial infections may be regarded as complications of the disease or as part of the disease process. Peptic ulceration reportedly occurs in 15 to 27 per cent of cases.[43] Emphysema frequently causes serious complications of pulmonary resection, especially bronchopleural fistula and empyema.[44]

Prognosis—The prognosis of emphysema is

more favorable for females than for males. It is more favorable if the onset is gradual rather than abrupt and late rather than early in life, if evidence of chronic cor pulmonale is minimal or absent, and if chronic bronchitis is a prominent feature.[3] Once the disease is disabling, only about 78 per cent of the patients survive for five years.[3] Once right-sided heart-failure is evident, few survive more than 12 to 18 months.

Clinical classification—We propose the following clinical classification of emphysema, which is based on severity of the disease as determined by history, physical examination and fluoroscopy:

CLINICAL CLASSIFICATION

0—No evidence of emphysema.

I—Objective impairment of ventilatory function with minimal or no symptoms.

II—Same as above plus moderate to severe dyspnea that is not incapacitating for gainful occupation.

III—Same as above plus physical incapacity for gainful occupation but no present or past right-sided heart-failure.

IV—Same as above plus past or present right-sided heart-failure.

Differential Diagnosis

Diagnosis of emphysema depends largely on a reliable history of dyspnea not caused by other conditions. The history is therefore considerably more reliable in diagnosis than is the physical examination. Radiologic findings and pulmonary function tests must be interpreted with care.[45]

The following conditions are commonly confused with emphysema: (1) various forms of heart disease, with or without congestive failure; (2) pulmonary embolism or infarction, especially when multiple; (3) hyperthyroidism; (4) chronic bronchitis; (5) localized bullous emphysema; (6) bronchiectasis; (7) bronchial asthma, especially the intrinsic variety; (8) incomplete bronchial obstruction due to tumor or tuberculosis; (9) pulmonary fibrosis, and (10) physical unfitness.

Emphysema is sometimes diagnosed by the surgeon when open thoracotomy is performed. The lung is hyperinflated, deflates slowly and incompletely when positive pressure is released by the anesthetist, contains frequent superficial bullae of varying size, and has a so-called "cotton candy" appearance. While there is good general correlation between operative and clinical findings, some cases are seen in which palpable and visible emphysema at operation is unassociated with any other clinical indication of the disease. We can explain this phenomenon in one of two ways: Either the operative finding is a fortuitous association of localized bullous emphysema and general bronchospasm, or the disease is in too early a phase to give clinical manifestations.

Treatment

Until the cause of emphysema is known, treatment will continue to be empirical. Even when all the facts are available, treatment doubtless will have to be *preventive*. Meanwhile it seems unlikely that medical therapy can do more than render symptomatic benefit and perhaps arrest the disease once it is fully developed.

These patients are frequently helped by stopping the use of tobacco.[23] However, if a trial of stopping smoking does not improve cough and lessen dyspnea the physician probably need not make an issue of the matter. A change of occupation may afford symptomatic relief. Various dusts and fumes tend to aggravate emphysema; the physical exertion required in some occupations may cause discomfort, although most persons who have fully developed emphysema cannot do any work.

Bronchospasm plays some part in the majority of cases. Hence, bronchodilators such as ISUPREL®, AEROLIN®, VAPONEPHRIN®, epinephrine 1:100 by inhalation, ephedrine by mouth, and aminophylline rectally all may be useful at times. Periodic rotation of these medications seems to enhance or preserve their effectiveness.

Mucolytic and wetting agents (steam, ALEVAIRE®) are sometimes helpful. The condition is made worse in some cases by excessive moisture, and in others by excessive dryness. An expectorant such as potassium iodide or ammonium chloride also may assist in this regard. Some patients are more uncomfortable

at high altitudes (above 4000 ft.) than at sea level, but the reverse is true occasionally and some patients are unaffected by a change in altitude. Much of the therapy of emphysema involves trial and error.

Intermittent positive pressure breathing (IPPB), using compressed air rather than oxygen, is a highly effective way to administer inhaled medications. The additional benefits ascribed to this procedure probably are largely psychogenic.[35]

The exsufflator or automatic coughing machine occasionally is quite useful in the short-term management of patients who are too weak to cough effectively and cannot get rid of secretion.[20]

Respiratory muscle exercises seem quite effective in many cases,[46,47] by reducing the inefficient motion of the spinal and shoulder girdle during respiration. Briefly, these exercises stress habitual forced expiration, as complete as possible, coupled with slow, quiet, incomplete inspiration. Objective evidence of benefit is difficult to obtain. Some investigators have noted that breathing exercises reduce the oxygen ventilation equivalent fairly consistently; the oxygen ventilation equivalent is an index of the amount of air the patient must breathe to absorb a given amount of oxygen.

Abdominal binders[48] or pneumoperitoneum,[36,49] or both, are sometimes employed in an effort to produce some pulmonary deflation and restore the diaphragmatic curvature in order to increase its range of motion. Pneumoperitoneum also may increase tussive force. Bronchodilators may have more effectiveness after pneumoperitoneum is established. Whether or not pneumoperitoneum will aid a given patient cannot be determined until it has been tried. Peritoneal adhesions, especially above the liver, may prevent any diaphragmatic change, and pneumoperitoneum then will simply cause pain and increase dyspnea. Usually the amount of gas injected is quite small when pneumoperitoneum is employed in emphysema, and the refills are also small (200 to 500 cc.) and frequent.

Infection plays an important part in most cases of advanced emphysema. Therefore, antimicrobial therapy is indicated for acute infections. Prophylactic chemotherapy, often for indefinite periods, not only makes sense theoretically but also works well in practice. Tetracycline, 250 mg. twice a day, appears to be a good agent for prolonged application.

Many emphysematous patients present the picture of right-sided cardiac decompensation. Textbooks often insist that digitalis is usually ineffective in this situation. Quite possibly digitalis has little effect on pure emphysematous right-sided failure in the absence of other cardiac disease. Right-sided failure may occur in part because of the coexistence of some other cause for myocardial weakness. In practice, therefore, digitalis sometimes is highly effective, frequently is beneficial, and seldom if ever is dangerous. Mercurial diuretics and sodium restriction very often are most helpful measures.

So-called medical thyroidectomy with I^{131} appears to offer some promise in advanced cases when the patient is unresponsive or no longer responsive to other therapy.[50] Presumably the benefit accrues from the reduction in the need for oxygen.

Table 1 summarizes an organized therapeutic approach to emphysema in the light of present knowledge.

Certain measures should be avoided in the treatment of emphysema. Morphine and its derivatives are dangerous because of cough suppression, retention of secretions, and depression of depth and rate of respiration. Rest in bed for most of the day, as might be advised for patients who have coexistent pulmonary tuberculosis, is contraindicated because of the danger of further loss of pulmonary function. This loss presumably stems from lack of stimulation of respiratory muscles. Collapse or resectional surgical procedures in the presence of emphysema should be undertaken with full awareness of the increased risk of complications and the reduced likelihood of a successful outcome.

Oxygen therapy is a double-edged sword. At times it is lifesaving and obviously necessary, but in some instances the lack of oxygen is the chief remaining stimulant to the respiratory center and oxygen therapy may further

TABLE 1

SYMPTOMATIC TREATMENT OF EMPHYSEMA

DISTURBANCE	METHODS OF TREATMENT*
Bronchial irritation	Stop smoking; avoid industrial fumes and smog.
Bronchospasm	Bronchodilators by mouth, rectum and inhalation (latter often with IPPB, using compressed air).
Retained secretions	Mucolytic agents; steam, expectorants; rarely tracheostomy.
Infection	Specific and prophylactic antimicrobial therapy.
Right heart-failure	Digitalis; diuretics; sodium restriction.
Disorderly breathing	Breathing exercises; abdominal belt; pneumoperitoneum.
Hypoxia	Inhalation of 40 per cent oxygen; I^{131} ablation of thyroid.
Carbon dioxide retention	Diamox; avoid oxygen, especially in high concentrations.

*Roughly in order of effectiveness; most effective first.

depress respiration. This tends to augment the serious problem of retention of carbon dioxide and the possibility of carbon dioxide narcosis and death.[1]

DIAMOX®, a carbonic anhydrase inhibitor, in doses of 250 mg. once or twice a day may afford temporary benefit by promoting the excretion of carbon dioxide.[39] Nevertheless its effectiveness is not very great and often is gradually lost. It may be dangerous.[46]

For patients with hypoxia and carbon dioxide retention the removal of secretions causing obstruction of the airway, often by bronchoscopy and occasionally by tracheostomy, may be the best approach in selected cases.

Steroid therapy frequently provides temporary symptomatic relief, especially for patients who have considerable bronchospasm,[51] but its use is fraught with uncertainties and is not recommended.[4]

Summary and Conclusions

1. Diffuse generalized pulmonary emphysema is a poorly understood disorder from the clinical, radiologic, physiologic and pathologic points of view.

2. Many cases of emphysema go unrecognized under various other designations, and likewise many other diseases are incorrectly labeled emphysema.

3. Emphysema is characterized clinically by severe dyspnea on exertion unexplained by other causes.

4. The history is a more reliable diagnostic criterion than the physical examination and single posteroanterior inspiratory chest roentgenograms.

5. Fluoroscopy is by far the most reliable diagnostic radiologic method, even including inspiratory and expiratory posteroanterior and lateral films.

6. It seems unlikely further improvements in methods of determining pulmonary function will answer the basic questions of etiology and pathogenesis of emphysema.

7. Further advances in knowledge of the microanatomy of normal and emphysematous lungs and discovery of a means to produce the disease experimentally seem to offer great promise.

8. The therapeutic approaches that are possible in the light of our present knowledge are discussed.

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Logistics of an Operation

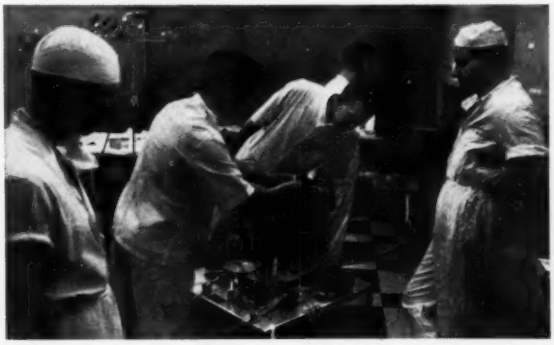
The day before the operation, the artificial heart is assembled. Above are screens over which the patient's blood will flow for the addition of oxygen and release of carbon dioxide.

Assembled, the apparatus is sterilized for 12 hours.

THIS pictorial feature was first published in *The Johns Hopkins Magazine* and was intended primarily for nonmedical readers. However, the Editors of POSTGRADUATE MEDICINE believe it will also have interest for professional readers and that it could be helpful when the need arises to explain the procedure to patients or their families.

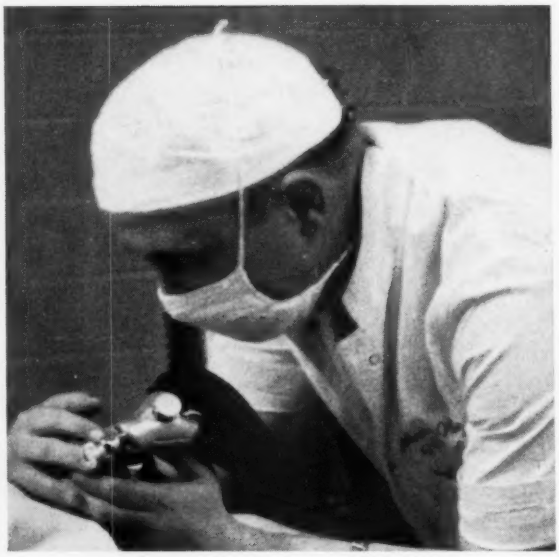
The operation being performed by the surgeons on the opposite page is one of the most delicate that has ever been devised. It was developed in order to repair a most serious congenital defect in the human heart: a hole in the septum, the muscular wall that separates one chamber of the heart from the other. To reach the site of the defect and stitch the hole, surgeons must work within the heart itself—a procedure that is not feasible as long as the heart is pumping blood. The solution: a mechanical heart than can take over the human heart's pumping functions long enough for surgeons to stop the heart's beating and remedy the defect.

The operation, now being performed regularly at Johns Hopkins and a few other hospitals, requires remarkable coordination and teamwork, not only among the operating team itself, consisting of four surgeons and a nurse, but also among 10 other persons in the operating room proper and numerous others outside, including engineers, technicians and 8 to 10 blood donors. On these pages are a few of the steps required before the blood of a patient can be detoured from his heart and pumped through the artificial heart—the complex and delicate logistics that precede the complex and delicate heart-patching operation itself.



On the morning of the operation, the heart pump, already checked thoroughly, undergoes a final inspection.

At the same hour, 8 to 10 donors are providing blood for the operation.

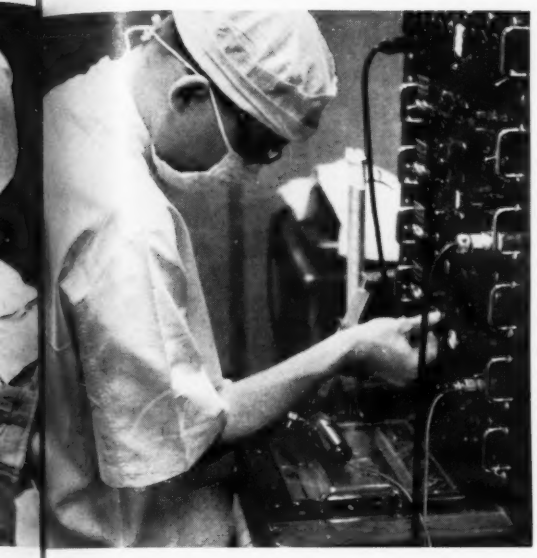


While the heart pump is on its way to the operating room, the patient is being prepared for surgery. Here the anesthesiologist administers anesthetic.

A quarter of an hour later, a cannula, or tube, is inserted in a vein for infusion of blood and intravenous fluids.

The speed of flow is adjusted in the recirculating pump of the heart machine. The patient's body weight determines the blood circulation rate.

The patient's chest has been opened. Throughout the operation, this operating room technician prepares needed instruments, using the sterilizer in wall.



In the operating room, a strain gauge, which records the patient's blood pressure via needles inserted in a vein and an artery, is calibrated.

Simultaneously, other operating room preparations move ahead: Drainage bottles are adjusted, saline solution is readied, and the surgeons assemble.

To estimate how much blood the patient is losing and how much must be replaced, an intern checks amount of blood removed by suction from the operating field.

Maintaining the patient's breathing, the anesthesiologist forces oxygen and anesthetic into the lungs via a tube to the windpipe.

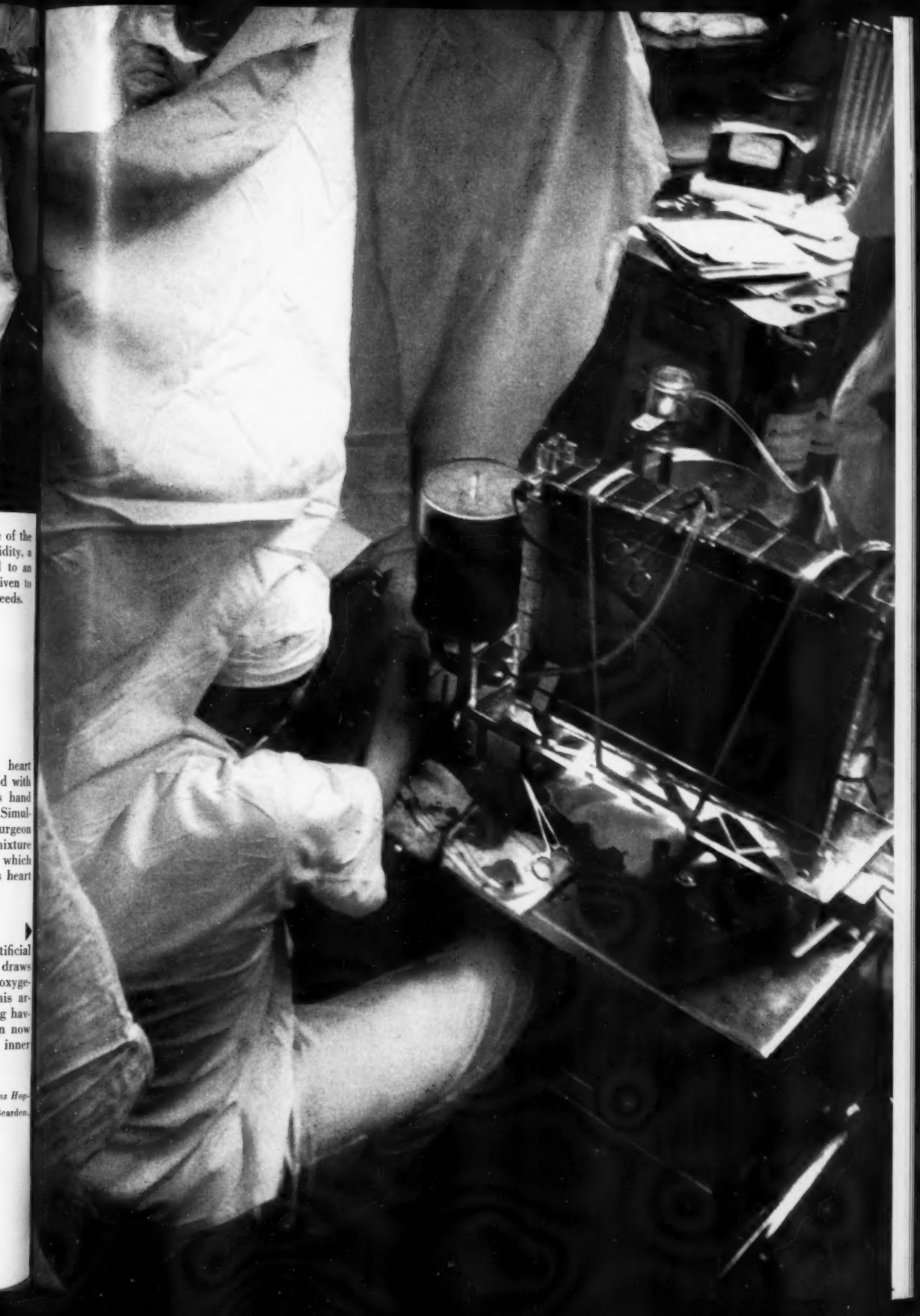
The patient has been in the operating room for about an hour. His heart has been exposed by incision. Now he is ready to be connected to the mechanical pump that will temporarily replace his heart. The tube in the picture will feed to an artery; another will tie in to a vein.

Working under a sheet, a surgeon draws a sample of the patient's arterial blood to measure its pH, or acidity, a guide to the patient's condition which may lead to an adjustment in the amount of ventilation being given to him by the anesthesiologist as the operation proceeds.

Now the actual tie-in with the heart machine is about to occur. Primed with blood, the tube in the surgeon's hand will be connected to the patient. Simultaneously, upper left, another surgeon prepares a syringe containing a mixture of blood and potassium citrate, which will be injected into the patient's heart to stop its beating.

The connection is made; the artificial heart takes over. One pump draws blood from the patient's veins; oxygenated, the blood is returned to his arteries by another pump. Its beating having ceased, the patient's heart can now be opened, and the hole in its inner wall can be repaired.

Reproduced with permission from *The Johns Hopkins Magazine*. Photographs by Alan J. Bearden.



The Use and Abuse of Pocket Nebulizers in the Treatment of Asthma

M. COLEMAN HARRIS*

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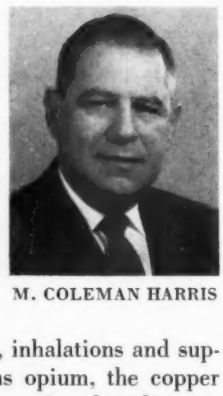

M. COLEMAN HARRIS

THE use and abuse of drugs or procedures in the treatment of disease are hardly new. Among the incantations, magic formulas and prayers in the remarkable Egyptian papyri of Kahun, the Berlin papyri, the Hearst Papyrus and the London Papyrus, there are prescriptions for gargles, inhalations and suppositories. Such drugs as opium, the copper salts and castor oil are mentioned, indicating that drugs were being prescribed as early as 1500 B.C. Some of these drugs were used with skill and understanding; others undoubtedly were not. Medicine was crude and primitive. Scientific safeguards were not available. Today, although safeguards exist in the form of laboratory assay and objective and clinical evaluation, the abuse of some drugs persists.

The abuse of a drug occurs most frequently (1) when it is a new drug and it has not been tested sufficiently to determine either all side effects or toxicity; (2) when the drug is so efficient in relieving pain or other distressing symptoms that it is taken more often than prescribed; (3) when, by relieving symptoms, the drug discourages further investigation which might reveal the actual cause of the illness; (4) when the drug, by stimulating the patient, producing euphoria or rendering him oblivious to reality, is taken when not therapeutically indicated, and (5) when the drug is sold without a prescription and consequently is taken without adequate supervision.

Inhalation is one of the oldest methods employed in the treatment of asthma. It has been used with steam alone, steam charged with

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drug vapors, or drugs finely subdivided. The radius of particles produced by steam inhalation is seldom less than 30 μ. Particles of this size do not penetrate further than the trachea. Therefore, steam inhalation is seldom of value in cases of asthma and is reserved chiefly for relieving the first stages of laryngitis or bronchitis. When a mist is produced with particles that have a radius of 10 to 30 μ., the process is called atomization. Particles of this size are able to reach the terminal bronchioles, but, if one wishes the medicament to reach the alveolar sacs, the particles must be even smaller; that is, they must have a radius of 3 to 10 μ.[1] Nebulizers have been devised to produce particles of this size.

The fundamental principle in the operation of most nebulizers is the passage of a jet or stream of gas across the top of a vertical tube immersed in a medicament solution. This produces a decrease in the pressure and causes the liquid in the tube to rise (literally be sucked up). Subsequently, it is broken up into small-sized particles and swept away by the stream of gas. In 1956, a new type of aerosol nebulizer (MEDIHALER®) was placed on the market. In this nebulizer the propellant providing the dispersing force functions also as the medium in which the medicament is dissolved or suspended. This inert propellant, which becomes a gas at room temperature and atmospheric pressure, exists as a liquid when confined under pressure in the nebulizer vial. A feature of this nebulizer is that when the specially designed valve is depressed a measured and reproducible dose of the solution is released. At atmospheric pressure, the propellant reverts to its normal gaseous state almost instantly.

The drugs most commonly used in pocket aerosol nebulizers for the treatment of asthmatic paroxysms are epinephrine, isomers of epinephrine, and isopropylarterenol or isoproterenol. Epinephrine has been shown to offer the best protection against the effect of histamine. Isoproterenol is claimed to be antagonistic to the effect of acetylcholine.[2] Many allergists believe that the isomers of epinephrine have no advantage over epinephrine. Antibiotics and mucolytic agents also have been employed in aerosol therapy, but these are better administered by nebulization by using an oxygen tank or an air compressor to provide more pressure than is available with the pocket nebulizers. In general, of the drugs used in pocket nebulizers, epinephrine and isoproterenol are exceedingly efficient in quickly relieving acute paroxysms of asthma. It is, therefore, odd an argument has been advanced that they should not be used.

There is no question about the absence of toxicity of epinephrine or isoproterenol. Their side effects are evanescent, are well known, and are acknowledged to be practically negligible. Actually, the argument centers around the fact that the efficiency of these drugs delivered by pocket nebulizers deters the patient from undergoing or completing an investigation to ascertain the cause of the attacks. The patient is thereby delayed from securing more adequate or specific therapy. One wonders if this contention is sound. A similar argument might be employed against the use of other drugs or remedies, aspirin, for example. Although this drug is used by thousands of people for the relief of headache, it never has been seriously questioned that aspirin should be withheld from sale because the persons taking it will tend to neglect undergoing an investigation to determine the cause of the headache. Morphine is habit-forming, but one would not hesitate using it for relief of extreme pain, if indicated. It would seem that, after fully explaining to the asthmatic patient that relief obtained by drugs sprayed into the bronchial tree by a pocket nebulizer is only temporary (something, incidentally, that the patient quickly learns by himself), and furthermore that it is being prescribed only for symptomatic relief, most patients would still desire further investigation to obtain more continuous and perhaps complete relief from attacks.

The argument that a nebulizer may be used too often and, therefore, may be harmful is not without merit. In the older types of nebulizers a wide variation in dosage is obtained, depending on the volume of the nebulizer bulb supplying the stream of gas and the strength or completeness with which the patient squeezes

it. Patients using this type of nebulizer undoubtedly are tempted to use it more often than they should in order to secure a proper amount of mist to relieve the attack. This is obviated, however, with the Medihaler, which delivers a single measured dose each time it is used. With the administration of a standardized constant dose, a single inhalation usually suffices, although two inhalations occasionally are necessary. More than this number seldom are required. Too frequent use of the nebulizer is prevented by describing to the patient the occasions when he should inhale the aerosol. It need not be used each time the patient feels mildly short of breath, but only when dyspnea actually is present.

Nevertheless, despite all such instructions, chronically ill asthmatic patients do tend to overdose themselves with aerosol by means of pocket nebulizers. This may be because they realize they have at hand a device which usually rapidly relieves their paroxysms. Admittedly, this is difficult for the doctor to control. Yet, this same circumstance is true in the use of other medicaments. How frequently we are told by patients that they took two tablets instead of one every four hours so as to double the effectiveness of the drug, or that they took the medicament every two hours instead of every four hours in order to obtain quicker action of the drug. Because this is frequently done, does it constitute a sound reason for not prescribing drugs? A pocket nebulizer should be placed in the same category as a tablet which can be carried in the pocket or purse of the patient for immediate symptomatic relief, similar to the nitroglycerin tablets which are taken by the cardiac patient when an attack of angina appears imminent.

The psychologic component in cases of bronchial asthma is often referred to in medical literature. In most instances, it is highly exaggerated. However, it is often clearly evident in cases of chronic asthma in which repeated attacks of suffocation have occurred. In such cases, the patients live in a state of apprehension, always in fear of another attack. The mere presence of a nebulizer containing an appropriate medicament, which from experience they know will give them almost instant relief, may help restore their equanimity and give them the sense of security they so sorely need.

The practice of allowing pocket nebulizers and the medicament to be used in them to be sold over the counter by druggists is a distressing matter. Their use definitely should be limited to the prescription by a physician who has examined his patient and feels that it would be helpful for the patient to have this therapeutic device. In many cases it may not be necessary.

If any one disorder were to be selected as singularly suited for inhalation therapy in acute attacks, asthma might well be chosen. During seizures, it is unique in being chiefly an expiratory dyspnea, with relatively effortless inspiration. In 1956 a study of 34 cases of chronic asthma* was made for the purpose of comparing the efficiency of the commonly used pocket nebulizers. In all but two of this series of cases, the patients obtained marked and almost instantaneous relief with the new measured-dose nebulizer. They preferred it to any of the other nebulizers with which corresponding tests were made. They did not have to use it as often. Furthermore, fewer inhalations were required when they did use it. This can be attributed to the metered-dose valve, which enables the patient to administer a constant dose on each occasion, and thus determine the minimal effective dose for himself. As a rule, one or two inhalations were sufficient to relieve the asthmatic attack.

These patients are still undergoing treatment. None refused to undergo the medical and allergic investigation which was advised when the pocket nebulizer was first given to them. Six have improved to such an extent that they no longer require any aerosol therapy. Eighteen still use the pocket nebulizer with epinephrine or isoproterenol, but only occasionally. Ten report that they still require the nebulizer as before. None use it in excess of the original instructions. All stated that having on hand an effective means of stopping

*The patients in these cases originally were observed in the Allergy Departments of Children's Hospital and in the Polyclinic Hospital and Postgraduate College, San Francisco.

an asthmatic attack gave them an increased sense of security.

Conclusions

1. The use of pocket nebulizers with sympathomimetic drugs for the treatment of acute attacks of asthma is efficient and generally reliable.

2. There is no toxicity with their use, and they have few, if any, side effects.

3. If the use of a pocket nebulizer is properly explained to a patient, it does not deter the patient from seeking investigation of the cause of the attacks and thereby securing specific and more lasting therapy.

4. Too frequent use of pocket nebulizers can be obviated by prescribing a nebulizer which administers a measured standard dose, and by specifying to the patient under what conditions the nebulizer should be used.

5. Overmedication with an aerosol delivered by pocket nebulizers probably is no more frequent than with any other medication which offers quick relief of distressing symptoms.

6. The presence of a nebulizer and an appropriate medicament in the pocket of an asthmatic patient is helpful psychologically.

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Books Received

Books received are acknowledged, and, as space permits, those of principal interest to our readers are reviewed more extensively. Reviews appear in this issue starting on page A-128; additional listings are on pages 155 and A-144.

Studies on Fertility. Includes papers read at the Conference of the Society for the Study of Fertility, London, 1956. Edited by R. G. Harrison, M.A., D.M., Derby Professor of Anatomy, University of Liverpool, Liverpool, England. Vol. 8 of the Proceedings of the Society. 138 pages, illustrated. 1957, Charles C Thomas, Springfield, Illinois. $5.00.

Clinical Electrocardiography; the Spatial Vector Approach. By Robert P. Grant, M.D., National Heart Institute, National Institutes of Health, Bethesda. 225 pages, illustrated. 1957, The Blakiston Division, McGraw-Hill Book Company, Inc., New York, Toronto and London. $7.50.

The Hangover. A critical study in the psychodynamics of alcoholism. By Benjamin Karpman, M.D., Chief Psychotherapist, St. Elizabeths Hospital, Washington, D. C. 531 pages. 1957, Charles C Thomas, Springfield, Illinois. $9.50.

The Year Book of General Surgery; 1957-1958 Year Book Series. Edited by Michael E. DeBakey, M.D., Professor of Surgery and Chairman, Cora and Webb Mading Department of Surgery, Baylor University College of Medicine, Houston. 560 pages, illustrated. 1957, The Year Book Publishers, Inc., Chicago. $7.50.

The Handicapped and Their Rehabilitation. Edited by the late Harry A. Pattison, M.D., former Director of The Potts Memorial Institute, Inc., Hudson, New York. 944 pages. 1957, Charles C Thomas, Springfield, Illinois. $14.75.

Mechanisms of Hypertension; With a Consideration of Atherosclerosis. American Lecture Series. By Henry Alfred Schroeder, M.D., Associate Professor of Medicine, Washington University School of Medicine, St. Louis. 379 pages, illustrated. 1957, Charles C Thomas, Springfield, Illinois. $9.00.

Bone Diseases in Medical Practice. By I. Snapper. M.D., Director of Medicine and Medical Education, Beth-El Hospital, Brooklyn, and formerly Professor of Medicine, Medical School of the University of Amsterdam, Amsterdam, Holland. 229 pages, illustrated. 1957, Grune & Stratton, Inc., New York and London. $15.00.

Liver-Brain Relationships. By Ian A. Brown, M.D., Associate Professor of Neurology, University of Minnesota, Minneapolis. 198 pages with 26 illustrations. 1957, Charles C Thomas, Springfield, Illinois. $6.50.

A Text-book of X-ray Diagnosis. By British authors. in four volumes. Edited by S. Cochrane Shanks, M.D., Director, X-ray Diagnostic Department, University College Hospital, and Peter Kerley, M.D., Director, X-ray Department, Westminster Hospital, London, England. Ed. 3, vol. 1. 521 pages with 533 illustrations. 1957, W. B. Saunders Company, Philadelphia and London. $18.00.

Fundamentals of Electrocardiography and Vectorcardiography. By Lawrence E. Lamb, M.D., Director of Cardiology and Chief, Department of Internal Medicine, Air University, San Antonio. 142 pages with 158 illustrations. 1957, Charles C Thomas, Springfield, Illinois. $9.50.

Clinical Gastroenterology. By Eddy D. Palmer, M.D., Lieutenant Colonel, Medical Corps, United States Army. 630 pages with 125 illustrations, 24 in color. 1957, Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York City. $18.50.

Selection of Patients for Group Psychotherapy

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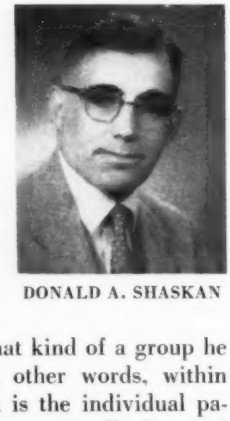

DONALD A. SHASKAN

THE acceptance of group psychotherapy as a major therapeutic technic has led to further research on some of the changing aspects of group dynamics and their effect on the individual patients. In any consideration relating to selection of group members one must give thought to what kind of a group he wishes to establish. In other words, within what sort of framework is the individual patient going to channel his emotionally distorted libidinal and aggressive drives?

Early workers in the field of group psychotherapy recognized that selection of group members is of key importance, and most of them expressed the need for great caution in this respect. As group therapy became less inspirational in character and more analytic, the early attempts to treat in one group patients having the same physical diagnosis, e.g., tuberculosis, hypertension or diabetes, were replaced by efforts to include in one group individuals with various complaints. This was done to increase the group's activity—so that initiative would pass through the group from one person to another. This mechanism relieves the therapist from the position of authoritarian leadership and places responsibility for cure on the individual patient, as he becomes able to assume it.

Bolder therapists varied the composition of the groups further by combining psychotic and neurotic patients. Some also considered handling the antisocial individual in a group and tried including such persons, but there was considerable reluctance to do this lest it jeopardize the integrity of the group.

In evaluating homogeneous groups versus heterogeneous groups one must keep in mind that less happens therapeutically in the former, due to the reduction in activity. In other words, heterogeneous groups tend to have more insight into the causes of emotional disturbance and to be more intuitive about the meaning and significance of group relation-

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ships, whereas homogeneous groups tend to fix their attention on objects external to themselves and bear a stronger resemblance to a work group.

As group psychotherapy has progressed steadily along lines extended from psychoanalytic research and findings, the tendency toward closed rather than open groups has become more prevalent; "open" denotes rapid change in the personnel among group members. This is readily understood, since controlled environment in the analytically oriented group becomes one of the prime essentials for deeper probing of drives and motivating forces and developing defenses against them.

Various technics have been developed to select patients for group psychotherapy. The report by our group[1] in 1950 was one of the first on the use of psychologic tests as a means of judging eligibility for group membership. At that time we were able to show only that the Rorschach test might help predict behavior in a group. The discussion dealt particularly with the case of a compulsive anal erotic with a rigid personality in whom moodiness, irritability, bouts of depression, and lack of self-confidence developed.

Moreno[2] developed sociometric means for predicting behavior in a group through a procedure which evaluates how individuals relate to those closest to them in a group situation. He observed that group psychotherapy experience proceeds more smoothly and effectively when the composition of the groups is based on sociometric choice.[3]

Powdermaker and Frank[4] facilitated the composition of groups by predicting the responses of one patient to another on the basis of relationship established during the initial interview and also on that of the patient's stellar position in the family. Striking a balance between inhibited and aggressive patients was one consideration given in the interest of group composition.

One cannot transpose to group therapy the same selective factors used in individual therapy. The ability to tolerate frustration which is of such prime importance in individual therapy plays a secondary role in group therapy, whereas the ability to withstand hostility, without which little could be accomplished in group therapy, is of minor importance in the individual (paired) therapeutic relationship. Desire for treatment is basic to both approaches, although those patients who remain in group therapy may seem to be more strongly motivated due to their acute realization of their own inadequacy in a social situation.

There is, of course, a marked difference between the selection of patients for an analytic group and that for a repressive-inspirational group. A person with a markedly dependent personality does poorly in an analytic group but is able to receive benefit in a repressive-inspirational group. The personality of the leader is less important in the analytic group as opposed to the dominant role it assumes in the repressive-inspirational group.

Six years ago I established at the outpatient mental hygiene clinic of the Veterans Administration in San Francisco a psychotherapeutic group which was permissive in nature, psychoanalytically oriented in interpretation, and largely closed to changing composition except for occasional replacement.[5] It was composed of neurotic patients and patients with mild psychoses who were receiving individual therapy as well. Selection was on the basis of intelligence and an interest in improving their adjustment at school or at work as well as at home. None of the members received psychologic or sociometric evaluation and none of the original patients had had previous group psychotherapy. Those who came in later had had group experience, however, and this experience had a direct bearing on the length of their stay in the group.

From its first meeting the group exhibited strong cohesion and great interest in understanding their own problems, which promptly became the group's problems. From the beginning there developed an extraordinarily good basic relationship characterized by strong feelings of identification and manifest efforts at cooperation.

For the purpose of this discussion I have selected 11 individuals who participated in the group—which, by the way, is still active. Six were in the group for four and a half years or more, and the remainder left the group

after from six weeks to a year. All except one patient in the latter category continued in individual therapy.

A brief description of the reasons for selecting these 11 patients for group psychotherapy follows. The first six are those who were able to remain in the group.

1. Selected because of intelligence and previous experience in group therapy and because he was a good treatment prospect.

2. Patient had been a subleader (patient-leader) in another group in the clinic. Assignment was made to this more challenging group when he seemed to be stalemated in his original group.

3. Referred to the group after spending several months in another group, where he was quiet and almost never participated. We felt that he would do better in a more stimulating and integrated group.

4. Patient had had previous group experience, was a good treatment prospect, and fitted into the cultural, educational and social background of the group.

5. Assigned to the group because of his sophistication, his ability to verbalize, and the ease with which he handled complex concepts. He had done a great deal of reading in psychologic and related fields.

6. Assigned because of his intelligence, social background and evidence of real motivation to work in psychotherapy and to handle emotional concepts. He had two unsuccessful attempts at concurrent individual therapy.

A brief outline of the reasons for referring those who left the group prematurely but not impulsively reveals certain peculiarities of adjustment which seemed superficial at the time but later showed our lack of comprehension of the depth of these symptoms.

7. Referred to the group because of native intelligence and good vocational adjustment. Also, there was no more appropriate group for him to enter at the time.

8. Patient, an Oriental, was chosen on the basis of his being a college student. Because of feelings of isolation, too, we thought this group sufficiently tolerant to accept a patient of another race.

9. A college student of superior intelligence was referred because of his need for socialization. After he left both group therapy and individual therapy, however, asthma developed. Ensuing individual therapy completely cured him but did not effect a basic personality change. He never returned to the group.

10. Assigned to this group when his individual therapist left. Previously he had been able to function in a group which made few demands on his passive attitude. It seemed to us that this group would answer his need for a more integrated social experience, but as soon as we were able to grant his request for another individual therapist he left the group.

11. Chosen on the strength of his ability to get along with his friends, this patient left both individual and group treatment following his divorce, when the group criticized his shifting relationships.

Significant qualities among the patients who remained in group therapy over a four year period which distinguished them from those who left were a strong motivation to get well, an ability to withstand hostility whenever the group focused it on them, an ability to verbalize feelings, and previous experience in group psychotherapy. By applying these criteria in analyzing the 11 members of the group, we see that the length of the stay of the six who had long-term group psychotherapy presumably is directly related to the presence of the above-named factors in a dynamic combination as compared with the isolated or unrelated existence of the five members who did not "last" in group therapy.

Since the ability to verbalize, to communicate in verbal exchange, as well as the trait of not being intimidated by verbal expressions of hostility were prominent factors in our related studies of patient-leaders (subleaders), we feel that an effort should be made to distinguish early those potential leaders among our patients. Although some leadership ability seems to stem from better personal or social adjustment, Powdermaker and associates have pointed out (and we have observed) that in other instances members assume a leadership role partly because of a greater degree of emotional illness. The near-psychotic's accessibility to his own unconscious may enable

him to perceive and interpret hidden meanings in what is going on, despite the fact that his own reality adjustment may be more faulty than that of the rest of the group who remain relatively unaware.

As we have pointed out previously, there are other qualities which both types of leaders possess. These include dominance, energy, facility in verbalization, and ability to withstand hostility. Leaders also tend to externalize anxiety; nonleaders tend to internalize it.

Sears[6] and Oettel[7] of our clinic have developed a scale of test items which gives promise of predicting whether or not a patient will assume a leadership role in group therapy. Patients are rated according to their responses to 50 true or false statements. This scale has been used successfully by us and by the Permanente Foundation in Oakland (not in prediction, however). There are indications that modifications of this scale may predict different kinds of leadership roles which a patient may assume in group therapy. Bion's[8] concept of dependent or fight-flight leaders may be explored in this connection.

Tim Leary[9] of the Permanente Foundation, in his search for methods of predicting behavior, has devised a circle of behavior characteristics. On the vertical axis are dominant and submissive behavior characteristics, and on the horizontal axis are characteristics between hate and love. Various tests can be quantified and scaled. As an example, we found that our patient-leaders were almost always more dominant and generally less hostile than our nonleaders. We are evaluating clusters in the circle to see if they may give clues of group therapy constellations.

Summary

Composition of an analytically oriented group for psychotherapy can be facilitated by bearing in mind the following qualifications: previous experience in group psychotherapy, a strong motivation to get well, ability to express emotions verbally, and ability to tolerate hostility engendered in the group. Knowledge of leadership and nonleadership factors aids in selection.

A group of 11 patients who participated in group psychotherapy is described briefly. In considering the patients who left the group it might be well to keep in mind that none of them could be considered in the category of "patient-leader."

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PHYSICAL MEDICINE AND REHABILITATION—*Sixth of a Series*

Use and Abuse of Ambulation Training in Rehabilitation

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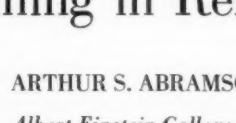
THE training of disabled persons to get about on foot is a well-established rehabilitative procedure. When used discriminately it affords functional and metabolic as well as obvious psychologic benefits. Some disabled persons do not have the physical capacity for developing safe, independent, effective and efficient ambulation. Safety means a stable standing posture and gait with minimal risk of trauma. Independence means the ability to do all things by oneself, without the help even of a wheel chair. Effectiveness means the capacity to walk long distances at a realistic speed, to walk up and down stairs, and to perform ambulatory tasks that are taken for granted in normal persons. Efficiency means that the energy reserve adequately exceeds the energy cost of ambulation.



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Programs with goals exceeding the patient's ability are an abuse of ambulation training.

To illustrate these principles I shall discuss several clinical situations associated with overt disabilities.

Osteoarthritis of the Hip

Osteoarthritis of the hip is so often equated with aging that one of its forms is called malum coxae senilis. However, it is the passage of time rather than age that is important in its pathogenesis. The local disease may begin early, but the clinical manifestations may appear much later.

Contrary to common opinion, osteoarthritis does not always seem to be the result of wear and tear.[1] In the hip, those portions of the joint surface that bear weight are preserved best and longest. Fibrillation of the cartilage and formation of osteophytes appear first and most commonly in the lower portion of the femoral head. This area bears weight only in extreme joint positions, positions not generally used for weight bearing. Only the upper portion of the femoral head bears weight consistently. This fact has been established by a close study of the anatomy of the joint and

of the bony stress lines in the head and neck of the femur which radiate to the shaft.

There is evidence that a pumping action produced by intermittent pressure on the cartilage of the weight-bearing area probably permits it to be nourished from a subchondral vascular bed.[2] The degree of pumping is less in the areas that do not bear weight, and this poorer nutrition perhaps accounts for the earlier destruction of their articular cartilage. A hitherto unknown phenomenon in aging bone and joints is the proliferation of new blood vessels accompanying the formation of osteophytes. With the passage of time the range of the joint becomes more restricted, weight-bearing areas become smaller and lines of stress more limited, and the cartilage on the weight-bearing portion wears away.

This sketchy outline of the pathogenesis of osteoarthritis of the hip provides clues to the prevention of crippling in this joint, or at least to its retardation. Ambulation affords range and intermittent compression in all but the very late stages of the disease. Excessive rest may be deleterious by diminishing the stimulus to joint preservation. Until recently, in keeping with the concept that osteoarthritis is a "wear and tear" disease, rest as a treatment for pain was not discouraged. However, prolonged maintenance of postures such as sitting may restrict the range of joints by producing contractures, and thus narrow weight-bearing areas.

Excessive ambulation may be damaging in late stages of osteoarthritis of the hip when weight-bearing areas have become small; this is especially true in obese persons. In this stage, surgical treatment or ambulation with an ischial weight-bearing brace may be attempted. In all stages, but most certainly in the late stages, excessive stress on joints due to obesity should be minimized by weight reduction.

Synovitis of the Knee

Atrophy of the quadriceps muscle commonly occurs rapidly after synovitis of the knee, whether the synovitis is due to direct trauma or a result of a surgical procedure.[3] This is true also in other disabilities involving the knee, such as those associated with rheumatoid arthritis. The probable cause of this atrophy is inhibition of muscular contraction due to the patient's fear of producing pain in the joint on movement.

Atrophy of the quadriceps muscle may produce an unstable joint. Stability of a joint depends on three factors:[4] the way the bones fit together, the ligaments binding them, and the muscles moving them. The fit of the bones in the hip produces sufficient stability to allow a scanty ligamentous binding. In the knee the fit is poorer and the result is a rich ligamentous endowment.

In a soggy knee joint with capsular stretching, ligaments are loose. If muscles are also weak and atrophied, use of the joint permits repeated microtraumas of slipping. This in itself produces synovial injury and thus sets up a vicious cycle. The surrounding muscles are the "court of last resort." Powerful and well-trained surrounding muscles can preserve the stability of a knee joint in which the ligaments are badly damaged. A damaged knee can be stabilized by training the quadriceps to a strength of at least two-thirds that of normal as measured on the opposite leg, thus permitting the regression of acute synovitis.[3]

Walking on a level surface produces minimal contraction of the quadriceps muscle and therefore minimal stimulation for its hypertrophy (figure 1). Obviously, walking up stairs or an incline is a greater stimulus to this kind of development. Persons with knee involvement who habitually strain the quadriceps on walking do better than those who do not. However, walking is damaging in the earlier and still weak stages of muscular hypertrophy. Strain exercises on walking are less effective at this stage than no walking until the quadriceps muscle is sufficiently strong. Such strength must first be developed through resistive exercises.

These principles probably are as valid in rheumatoid arthritis as in traumatic synovitis, but many factors complicate the former condition. The surfaces of the joints are relatively well preserved in traumatic synovitis, but in rheumatoid arthritis there are inflammatory destruction of cartilaginous surfaces and cystic

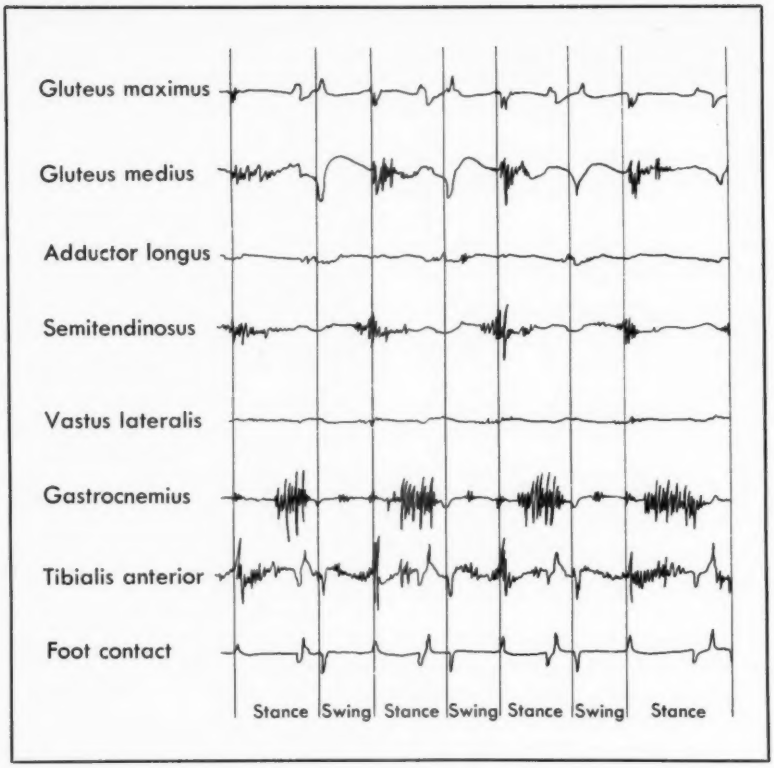

FIGURE 1. Simultaneous electromyographic tracings of normal lower extremity on level walking. Muscular contraction continues during a fraction of stance-and-swing cycle. Quadriceps contracts only slightly.

changes in the subchondral bone. It is difficult to determine if weight bearing can maintain articular cartilage in this condition as it does in osteoarthritis of the hip, because pain and illness prevent walking and the institution of exercises. Contractures also occur rapidly because of long-maintained postures produced by pain and muscular inhibition.

It is good practice to persist in walking to the limits of residual pain after analgesia and in the absence of marked constitutional illness. Walking with unsupported and unbraced joints in the late stages of joint destruction is unquestionably damaging. Any form of walking may be damaging without previous preparatory exercise to stabilize joints by strengthening muscles.

Amputation

Gangrene due to occlusive arterial disease is the most common cause of amputation, and the most frequent peripheral arterial disease is arteriosclerosis. This disease requires time to develop to the point of producing a clinical disorder. Thus, while arteriosclerosis is not necessarily a disease of the aged, most amputees are elderly persons.

In the past, age was considered a barrier to prosthetic rehabilitation. It was a common clinical impression that if a unilateral amputee more than 55 years of age were to walk with a prosthesis and if he had arteriosclerosis and especially diabetes, gangrene and loss of the other limb would ensue rapidly. This view is not in accord with more recent experience. Some clinicians have even advocated ambulation in the presence of limited dry, uninfected gangrene.[5]

Buerger's exercises do little to increase available circulation in occlusive arterial disease, but exercises against resistance are more likely to accomplish this.[6] Although this prin-

ciple has been established only for circulation in calf muscles, it is likely that it applies also to circulation in other tissues in the lower extremity, such as the skin. Few forms of exercise can supply this stimulus to increased circulation as well as walking.

With meticulous care of the feet and protection of the remaining limb against injury, prosthetic ambulation is quite safe at any age as far as loss of the remaining limb is concerned. Eventual loss of the other limb may be inevitable, but walking may delay it. Age, arteriosclerosis and diabetes are not by themselves obstacles to ambulation training. Only severe reduction in cardiorespiratory reserve and severe ischemia in the opposite limb can be considered substantial, but not absolute, contraindications.

Aging frequently reduces energy and cardiorespiratory reserve, especially in the presence of vascular disease. These are important considerations in ambulation programs for elderly amputees. For normal persons, walking on a level surface requires little energy expenditure, since muscular contraction ordinarily lasts through a fraction of the stance-and-swing cycle (figure 1). This is not the case with an amputee. A short stump and circumscribed muscle masses such as those surrounding the hip are required to perform tasks such as activating a lifeless, heavy limb. Proprioceptive and kinesthetic senses that once contributed to efficient maintenance of balance are now lost, and additional muscles must contract to maintain balance. Substitutional motor activities are less efficient than normal ones. These activities are even more costly for the bilateral amputee, for those with above-the-knee amputations compared with below-the-knee amputations, and for amputees in whom flexion contractures of the hip have developed. An upright stance is well-nigh impossible for the bilateral above-the-knee amputee with flexion contractures of the hip and without youthful flexibility of the lumbar spine permitting a compensatory lordosis. If such a person wears prostheses and uses crutches in order to stand, the expenditure of energy obviously is quite excessive.

Improved prosthetic rehabilitation has resulted from the early institution of physical treatment, even before amputation, and from the trend to amputate below the knee rather than above the knee, as was once done routinely. While any rehabilitative program requires careful clinical evaluation of reserves, excessive conservatism often is practiced at the expense of a fuller, happier, more active life for the amputee. If the aforementioned principles are observed, ambulatory rehabilitation of the elderly amputee is safe.

Early restitution of ambulatory function can prevent certain complications of amputation. Among them are contractures of joints and phantom pain. Too great a delay between operation and rehabilitative measures may permit the development of a weak, persistently flabby stump, and contractures of the knee and hip in below-the-knee amputees and of the hip in above-the-knee amputees. The presence of stump and phantom pain may hasten the formation of contractures. In the knee the only possible deformity is flexion. In the hip, partial surgical destruction of the adductors with preservation of the abductors, partial destruction of the hamstrings (which are strong hip extensors), and preservation of the hip flexors will favor formation of abduction and flexion contractures in above-the-knee amputees. Prolonged sitting in a wheel chair predisposes more readily to these deformities.

Early treatment including bandaging of the stump, exercising of muscles and stretching of joints may be instrumental in preventing these complications. Even more effective is early pylon ambulation, begun as soon as the wound heals and the sutures are removed.[7] Pylons are cheaply and easily fabricated with stockinet, felt, plaster of paris and walking irons (figure 2). Early institution of this kind of function appears to eliminate phantom pain entirely and to reduce stump pain considerably.[8] Wearing of the pylon prevents contracture by the mechanical stretching process of ambulation, shrinks the stump more rapidly and adequately, and permits the development of stronger and better-coordinated muscles through functional use.[7] Some observers believe that pylon ambulation teaches poor gait patterns. It is hard to conceive that what was

learned so quickly could not be as quickly discarded in later training with a jointed permanent prosthesis. The advantages of pylon ambulation far outweigh any temporary disadvantages.

FIGURE 2. Plaster pylon.

Hemiplegia

Just as arteriosclerosis is the most frequent peripheral arterial disease resulting in amputation of the lower extremity, so the most common form of hemiplegia is associated with arteriosclerosis. Some of the principles previously outlined apply equally to both the amputee and the hemiplegic patient, since the latter is usually older and has reduced reserve, with extensive vascular disease often involving the heart and peripheral vessels.

Early ambulation usually will give a better functional result. Delay in instituting rehabilitation of hemiplegic patients may permit development of unmanageable spasticity. Long periods of rest in bed and inactivity in a wheel chair may result in flexion and external rotation contractures in the involved lower extremity. While passive and active exercises can effectively prevent these complications and stimulate return of function, weight bearing and ambulation are far better stimuli. It is not unusual for a hemiplegic patient who exhibits no voluntary movement of the limb while being examined in the supine position to show some movement when upright, even to the extent of being able to lock the knee.[9] A splint may be necessary to maintain the upright position, but training in this ambulatory position leads to more rapid recovery of walking function and the splint may be quickly discarded. Moreover, resumption of ambulation usually terminates incontinence unless extensive bilateral cerebral damage is present.

To walk safely, the hemiplegic patient who has residual paresis may require a short leg brace, or drop-foot brace. Neglected hemiplegic patients whose training starts late and in whom spasticity is severe and flexion contractures of varying degrees have developed may need a long leg brace permanently, and even then the functional result may be relatively poor (figure 3).

Because of the cerebral damage and spasticity, the gait which the hemiplegic patient develops, either spontaneously or through training, may be bizarre. A stiff-legged, circumduction-abduction, equinovarus type of swing phase is common. Many institutions do not consider this form of walking acceptable. Patients are supplied almost routinely with drop-foot braces to bring the foot to a right angle and permit it to clear the ground without tripping. Then, instruction is given in a laboriously performed but cosmetically better-looking gait. The result of this kind of training is questionable, and therefore the training itself should be questioned. If normal-appearing walking were easy to perform and if the

FIGURE 3. Patient referred for rehabilitation about eight months after a stroke. He required a long leg brace, and ambulatory function after training was limited.

hemiplegic patient felt safe with it he would rapidly assume it with only minimal training. It may be that the bizarre gait is safer and more efficient.

Use of a brace can interfere with the natural rhythm of the newly integrated gait and occasionally even with stability. If the foot clears the ground without tripping, either with or without an elevation on the opposite shoe, and if the patient places the foot flat on the ground, a brace is not indicated even in the presence of some equinovarus deformity. If persistent walking renders the gait more unstable because of fatigue, a brace is indicated. The important consideration in regard to the use of a brace is the presence of an unsafe gait; when the gait is unsafe, a brace should be supplied.

For any spastic person who has enough volition to walk, the energy cost of doing so is greater than it is for normal persons. Spasticity permits the irradiation of impulses produced by movement not only to those muscles whose integrated action performs the movement but even to antagonists and to muscles ordinarily not concerned (figure 4). The spastic person uses even the normal opposite limb more stiffly than is necessary in the absence of disability.[10] This constitutes excessive use of muscles and therefore an excessive energy cost. It explains why a person whose spasticity is severe tires so much more quickly than one with less disability. It also explains why it is wise not to train the elderly hemiplegic patient toward a goal of normal speed and distance in walking.

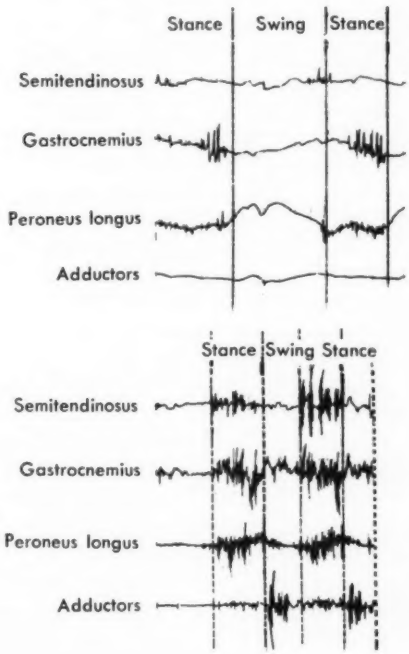

FIGURE 4. Simultaneous multichannel electromyographic tracings of a normal lower extremity *(top)* and a spastic lower extremity of a hemiplegic patient. Excessive muscular contraction is noted in the spastic limb.

Paraplegia

Knowledge concerning the rehabilitation of persons who have transverse lesions of the contents of the spinal canal was derived largely from experience with young war veterans. For this reason, less attention has been paid to the energy cost of ambulation.

When rehabilitative programs were first established for paraplegic patients, training goals of total brace-and-crutch ambulation were set. To the surprise of the therapists, the programs were far less successful than they had hoped. At first this was attributed to the lack of motivation and other emotional factors in the face of an obviously formidable goal. Then certain physical factors were recognized as being important. The patient who had a low lesion in the cauda equina, with flaccid paralysis limited to the lower extremities and hips, could be taught to ambulate more safely, independently and effectively than the patient who had a high spinal cord lesion with spasticity. The former patient also could be trained to walk further, faster and with less fatigue, although the gait would be slower than normal and his endurance less.

Efficiency of gait in paraplegic patients depends on the level of the lesion, being greater in lower lesions and less in higher ones. Studies have shown that a major factor in energy reserve is the residual functioning muscle mass. The more such tissue is lost through amputation or paralysis, the less the energy reserve.[11] Damage to the cardiorespiratory apparatus, another possibility in the reduction of energy reserve, usually is not a factor in young patients, but it is an important consideration in later years and in older paraplegic patients.

In order to walk, the paraplegic patient uses his upper extremities and shoulder girdle. They are poorly adapted for this substitutional function, and even with the best of training (which in itself gradually reduces the energy cost of any performance) walking requires a considerably greater expenditure of energy than it does with intact lower extremities. Loss of sensation in the lower part of the body also makes it necessary for muscles under voluntary control to work harder just to maintain balance. That is why ambulation is so much more successful in paraplegia due to poliomyelitis, in which case sensation is preserved. It is obvious that paraplegic ambulation can be made safe only at considerable expense to the organism.

Obesity and the weight of braces add to the energy cost, as does a more severe degree of spasticity. The margin between energy reserve and energy cost in paraplegic ambulation is so greatly reduced that walking at even as slow a rate as a mile an hour can be compared to running by the normal person.[11] Obviously most paraplegic patients are unable to do this all day long.

Yet ambulation has advantages for paraplegic patients. It reduces spasticity in some instances, prevents contractures, exercises muscles, and prevents osteoporosis and calcium loss from bones, bone fragility, formation of calcium urinary stones, and ossification of soft tissues.[12] It aids in urinary drainage when the patient has a neurogenic bladder. It enables the paraplegic patient to get places inaccessible in a wheel chair.

Thus, ambulation training in paraplegia is useful if it is judiciously combined with wheel chair locomotion. In most cases, attempts to develop complete ambulation constitute an abuse of this form of training.[13]

Summary and Conclusions

Ambulation can be either beneficial or harmful. It can preserve tissue or damage it, depending on the available reserves and the price of the ambulation goal. Acute constitutional manifestations of rheumatoid arthritis, extensive vascular disease, reduced cardiac and respiratory function, advanced joint destruction, extensive amputation, and marked motor paralysis reduce the reserve. Such factors as disuse atrophy of muscle, lack of training, contracture of joints, sensory loss, obesity and spasticity increase the price. Delay in establishing rehabilitative procedures further intensifies these factors.

Since many diseases begin early and become manifest late, the effects of disease are more important than age itself in evaluating

reserves and costs. If reserve is considerably greater than cost, useful ambulation is possible and the patient should be trained for this goal. With a lower reserve and greater cost the ambulatory goal must be commensurately less. No clinical method yet devised will replace experience and judgment in determining reserves and costs. Excessive conservatism should be avoided, but at the same time overoptimistic expectations may lead to frustration for both patient and doctor.

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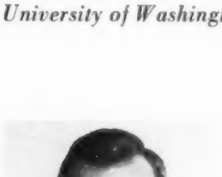
CASE REPORT

Functional Heart Murmurs

GREGORY G. JOHN*

University of Washington School of Medicine, Seattle

I SHALL report a case which will illustrate the importance of functional heart murmurs.



GREGORY G. JOHN

Case Report

A cardiac murmur was first heard in a girl three days after her uneventful birth. During childhood, growth, development and activity were normal, but she tended to be underweight. When she was 11 years old, she was constantly fatigued, exertional dyspnea was present, and her temperature occasionally reached 99° F. On this basis, a diagnosis of acute rheumatic fever was made without the major diagnostic criteria, and she was rested in bed for four months. During this time, she gained 15 lb. and improved in strength and appearance. When activity was resumed, there was a recurrence of the fatigue and tachycardia. A more complete cardiac evaluation, therefore, was undertaken.

At the age of 12 years, she was a large, clumsy, apprehensive girl who had reached puberty. Tachycardia was present, but there was no evidence of cardiomegaly. A faint systolic thrill was palpable in the second and third intercostal spaces on the left side. The second pulmonic sound was accentuated. A grade 4 systolic murmur was audible in the pulmonic area. The intensity of the murmur decreased during inspiration but increased during expiration. The electrocardiogram was consistent with the evolving right heart pattern of childhood, but depression of the ST segment suggested the presence of subendocardial ischemia. The circulation time was seven seconds when determined with Evans blue. She responded to standard exercise with clumsy activity and by an increase in the heart rate to 195 beats per minute.

A presumptive diagnosis of patent ductus arteriosus was made despite the absence of a continuous murmur. Cardiac catheterization was not entirely satisfactory, but data obtained at different times seemed to be consistent with the presence of a patent ductus arteriosus. Thoracotomy revealed that the ductus was a ligament. Intrapericardial exploration did not disclose any structural cause for the thrill and murmur which persisted.

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After the operation, she led a protected life at home, and a private tutor was engaged. The child's activity was limited, and she slept at least 12 hours each night. A year after the operation, the generalized cardiac awareness of the family was illustrated by the mother's concern over the child's failure to grow, although she had grown 3 in. and had gained 25 lb. in the meantime. The results of physical examination were the same as they had been at the time of the operation. There was evidence of hyperactivity, hyperkinemia and hypermetabolism without hyperthyroidism. The child expressed a keen desire to be more like other girls of her own age.

It was finally concluded that the child had a functional murmur, and the difficult task of reassuring the family and the child was undertaken. She was permitted to resume normal activity slowly. Reserpine was administered for its bradycrotic effect. In the course of the next year, she was returned to her just place in society. She was able to engage in the normal activities of a 14 year old girl without the occurrence of unusual symptoms. When she had acquired poise and the administration of reserpine had been discontinued, the pulse rate was 70 per minute while she was resting, which was the same rate that had been obtained with the administration of this drug. When the heart was beating at this rate, a soft, grade 2 systolic murmur was audible in the pulmonic area, and the second pulmonic sound was slightly accentuated.

Comment

This case has been reported to demonstrate that a functional murmur is not always literally benign. The combination of a benign murmur and puberal development led to marked physical restriction, and to the performance of a potentially dangerous diagnostic procedure and a thoracic operation. The psychic trauma may yet result in a severe cardiac neurosis.

A consideration of functional murmurs, therefore, is of more than academic interest. Only with a knowledge of normal heart sounds can one recognize abnormal sounds, and only with a knowledge of nonsignificant murmurs can one recognize significant murmurs.

Cardiac murmurs are abnormal vibrations in the cardiac cycle with a frequency of 50 to 500 cycles per second; they result from development of turbulences in the laminar flow of blood.[1] Fluid may flow through a tube at a given rate without disturbing the layering effect or laminar flow until a certain critical speed is exceeded, when currents and eddies develop and result in a murmur.[2] Disruption of laminar flow may occur with deformity of the flow pathways in the absence of increased velocity of flow. This disruption occurs: (1) in cases of dilatation beyond a valve in the pulmonary artery or beyond a valve in the aorta in cases of aortic aneurysm; (2) in cases of dilatation of a valve itself (valvular insufficiency); (3) in cases of constriction of the outflow (valvular stenosis or vegetative endocarditis); (4) in cases of abnormal shunting (patent ductus arteriosus and septal defects), and (5) in cases of a movable flap (rupture of valve cusp or papillary muscle).

Disruption of laminar flow may occur with increased velocity of flow without deformity of the flow pathways. This may be associated with hyperthyroidism, anemia and exercise. In this type of disruption, turbulence is not secondary to dilatation of the valve and relative insufficiency, as is well illustrated by roentgenograms which are made after exercise. Such roentgenograms have demonstrated that the heart is no larger than normal and may even be smaller, despite the development of a murmur. This increased velocity may be apparent only in the proximal portion of the aorta or pulmonary artery. Levine[2] has said that these murmurs may be produced because the blood is ejected from the root of the great vessels with a "snap." Other conditions may disrupt the laminar flow, but they are not intrinsic deformities of the flow pathways. These conditions are: (1) dilatation of the pulmonary artery secondary to exercise or Valsalva's maneuver; (2) kinking and twisting of the pulmonary artery with a change of the position of the heart or an increase in cardiac output or thoracic pressure,[3] and (3) deformity of the flow pathways resulting from extrinsic masses such as hilar lymph nodes or a depressed sternum.

Functional heart murmurs have been designated by such terms as physiologic, nonsignificant, benign, nonorganic and nonpathologic. The implication of all of these terms is that the murmur is not caused by distortion of the flow pathways, but is due to the increased velocity of flow.

Functional murmurs are relatively rare during infancy. At this stage of life, murmurs usually are associated with other signs that point clearly to the existence of congenital heart disease. The incidence of systolic murmurs in infants is somewhat less than 2 per cent. These murmurs presumably are not due to a patent foramen ovale or a patent ductus arteriosus, because these defects are present in a far larger percentage of infants.[4] The exact site of these murmurs is unknown, but it is surprising that turbulences do not occur more commonly at a time when radical changes are occurring in the circulation. By the end of the first year of life, the incidence of systolic murmurs is about 7 per cent.[1] From this time on through childhood and adolescence, the incidence of murmurs increases rapidly, and the absence rather than the presence of a murmur may occasion surprise.[5] According to various authors, the incidence of such murmurs ranges from 12 to 60 per cent, but it probably is between 20 and 30 per cent.[6]

There are two major functional murmurs, namely, Still's murmur and the pulmonic systolic murmur. Still's murmur, the precordial vibratory or "twanging string" murmur, lies medial to the apex and usually lateral to the left border of the sternum in the region of the fourth intercostal space. This murmur comprises about a third of functional murmurs which occur in childhood. It decreases in intensity during adolescence and disappears by adulthood. The pulmonic systolic murmur, which comprises about two-thirds of the functional murmurs which occur in childhood, decreases in intensity and radiation with age. In cases in which it persists until adult life, it is confined to the pulmonic area.

Phonocardiographically, the systolic murmur of valvular insufficiency is so complex that no fundamental frequency can be determined. The phonocardiogram of the precordial vibratory murmur (Still's murmur) discloses a simple uniform wave of constant frequency resembling a damped sine wave of 70 to 130 cycles per second. The pulmonic systolic murmur of functional nature is intermediate between these two murmurs. It consists of a basic simple wave with superimposed distortion, but it is not chaotic in character.[7] The functional murmur is systolic in time, follows the first sound after a brief pause, and extends only through the second third of systole. The murmur of valvular insufficiency begins immediately after the first sound, without any silent interval, and extends through systole.[8] A functional murmur is buzzing, like a vibrating string, or is blowing in character. It usually is faint in intensity, and never is more than moderately loud (grade 3). It may be transmitted to some extent, but not far. It is loudest when the patient is recumbent, and diminishes in intensity or disappears when the patient is sitting or standing. It frequently disappears during deep inspiration, or diminishes in intensity and becomes loud again only after the heart has taken a few beats. It usually becomes louder after effort, and in a few cases it occurs only after exercise.[9] A functional diastolic murmur is a rarity, and it presumably occurs only in cases in which anemia has resulted in cardiac dilatation.

Venous hum is another thoracic noise which occurs commonly and may be mistaken for a cardiac murmur. This is a continuous roaring or blowing which occurs throughout the cardiac cycle and is augmented during diastole.[10] It is heard best at the root of the neck, particularly over the jugular vein on the right side. It is loudest when the patient is erect, and it diminishes in intensity or disappears when the patient assumes the recumbent position. It is loudest during inspiration, when negative intrathoracic pressure hastens the return of venous blood to the heart. It increases in intensity when the head is turned away, and it disappears when sufficient pressure is exerted with the bell of the stethoscope to obliterate venous patency. It frequently is transmitted downward to the precordium, and it then may mimic the continuous murmur of a patent ductus arteriosus.[10]

Murmurs associated with cardiac symptoms, roentgenologic evidence of cardiac enlargement, or an abnormal electrocardiogram should be considered significant. Even without these ancillary findings, a murmur is likely to be significant if it is louder than grade 3, if it is of appreciable duration, if it is transmitted well throughout the precordium, the neck and back, and if it is not influenced by the phases of respiration or by change of position.[1]

A functional murmur never causes true cardiac symptoms or laboratory evidence of heart disease. It usually is of low intensity and frequency, of short duration, and occupies midsystole. It is of maximal intensity in the pulmonic area or parasternally. It is transmitted poorly, and it varies considerably from cycle to cycle with respiration and change in position, or for no very obvious reason.

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Postgraduate Clinical NOTES

89. REST AFTER CORONARY THROMBOSIS

The question of bed rest is a matter of considerable importance. In the practice of geriatrics it is generally accepted that activity should be encouraged and there are few indications for confining a patient to bed. In the case of the patient who has had a "heart attack," however, the view is so firmly held by many medical practitioners and by members of the lay public that complete rest in bed for four to eight weeks is essential that should anything untoward happen to the patient while he is out of bed then the physician will be considered blameworthy. Yet, in fact, not only are complications more likely to occur if the patient is kept in bed but also it has recently been shown by catheterization studies that the work of both the normal and the diseased heart is 23 per cent greater in the recumbent position than when the patient is in a chair with his feet down (Levine, 1955). Thus, for most patients who have sustained cardiac infarction, or who have congestive cardiac failure, it is more effective to treat them in a comfortable chair with their legs in a dependent position. The only contraindications are extreme weakness or symptoms of cerebrovascular insufficiency associated with hypotension.

A. N. Exton-Smith, Advances in geriatrics, *Practitioner*, October 1957, p. 442

The Quacks of John Hunter's Time

A. DICKSON WRIGHT

London, England

Prologue

To give this oration on a subject apart from your life and work requires an explanation to you, our patron saint and example, John Hunter.

We of this Society who cluster round your memory are always thinking of you and reading of you. We know your fortes and your foibles. We think of you as a boy on your farm in Lanarkshire, with the mysteries of nature ever in your mind, so that your school attendance suffered. We know that when you threw your leg over your old farm horse on an autumn day in 1748 and rode all the 400 miles to London, you were almost illiterate. In view of your future erudition, we trust that this will not be used as a defense for our modern system of subsidized illiteracy. We know that when you arrived first in London, you kept bad company; you allowed your honest name of John to become the sinister one of Jack, and the stews and stage doors knew your face and the resurrection men, your company. But then you were only 19 and you had not brought your mother with you, and, possibly, without this experience, you might not have made your valuable contributions to the study of venereal disease.

We know that you studied with Percivall Pott and Cheselden and did house posts at St. George's, and, when you had the usual hemoptysis of the times from overwork, you joined the army and served in Belle Isle and Portugal. You did not then spend your time at cards and gossip in the mess anteroom, but continued to work hard amidst all the distractions of army life, studying gunshot wounds, inflammation and the mysteries of hibernation.

We know that when you returned to England and resumed your teaching, that your lectures lacked the fluency of your brother, and you needed a little swig of laudanum to inspire you before you started. We cannot criticize you for this, because we know that laudanum gave us "Kubla Khan" and the "Bride of Lammermoor" and many other masterpieces, which we do not hesitate to enjoy, and, moreover, our present national expendi-

Oration delivered at the Mansion House, London, to the Hunterian Society and reprinted with permission from the *Transactions of the Hunterian Society*, Vol. XI, pp. 68-83.

ture of a thousand million a year on tobacco and alcohol should make us uncritical. We know that your lectures were poorly attended as were those of Lord Lister and even those of this year's orator, but your attendances were of good quality; Astley Cooper, Anthony Carlyle, Abernethy, Clive, Jenner and Macartney, all sat at your feet, and even some of the successful rascals of whom we speak tonight.

We know that you were quarrelsome, but that was the custom of the age. Your quarrel with your brother over plagiarism would not have taken place in this day of teamwork when the head of the department publishes the discoveries of his juniors, and you would probably have figured without complaint as the humble et al. of the present day. However, it was very naughty of you to kick out of your drawing room the arty and crafty types at your wife's "kickup," but I am sure there are one or two in tonight's audience who would love to do likewise on occasion.

We know that all your researches were paid for by the money you earned in your own private practice, and yet you discovered more than all the subsidized research of the present day. We know that in your insatiable thirst for knowledge you even went to the extent of infecting yourself with two loathsome diseases, knowing full well the years of painful and miserable treatment that would follow, but this is more excusable than some of the researches made on animals, patients and "volunteers" at the present day.

We know that the judge ignored your evidence when you went to court, but they have never liked our profession and still show a certain waywardness in medical matters. We know that you were a die-hard Tory and held that those who did not like the country could leave it! So we are glad you were spared the welfare state, where industry is a crime and nothing fails like success.

When your end came, it was at a frustrating, aggravating committee, and we of this age who spend half our life in smoke-laden committee rooms sometimes yearn for a similar escape or, better still, a similar fate for our aggravators.

The story of all these things and many more has been told in orations of the past, and now we would turn to the study of the age and contemporaries in which you were set and so to admire your work the more.

The eighteenth century has been well described as the Golden Age of Quackery, and England, as the Paradise of Quacks. Now the eighteenth century is one in which the British surgeon has very considerable interest, because it is the century of John Hunter. The enthusiastic Hunterian never hears the name of a notability of that period, without wondering the contacts he had with his Hunter, and Hunter had great and picturesque contemporaries. There were Hogarth and Joshua Reynolds, Samuel Johnson and Boswell, Robert Burns, Pope, Garrick, Sheridan, Rowlandson and Gillray, the Walpoles and Fox. The details of everyday life of London in the eighteenth century interest the true Hunterian. Never do I walk past Fortnum and Mason's, the Odeon Cinema in Leicester Square, and the Windmill Theatre, but I think of Hunter. I think of him coming out of his door and walking down toward St. George's Hospital. I wonder what the road surfaces looked like, was it really unpaved; did the passers-by recognize him and give him the time of the day; did he ever pass Admiral Nelson with Lady Hamilton on his arm, making his way down Arlington Street to St. James's to buy a new hat at Lock's or some wine at Berry's; did he ever see the besotted Sheridan emerging from Buck's after an all-night carouse?

He lived in days of fierce professional competition; much depended on the favors of the wealthy, autocratic aristocrats, who suffered from a high mortality rate, owing to the high rate at which they lived. The demise of one of these caused feelings to run very high, and very often bitter controversy would break out, and pamphlets and counter pamphlets would be issued of criticism and explanation. Such a one attacking William Hunter is in our library and concerns the death of Lady Holland and is written by Dr. Rowley. We know a great deal of Hunter's professional rivals, but it is also useful for a visualization of the period to study Hunter's unethical competitors. These were all too ready to claim acquaintanceship

Kneller's portrait of a famous eye quack of Queen Anne's time. He practiced in partnership with his wife, and they did not confine their activities to diseases of the eye.

with the famous man and even to state that they had been his pupils. There was certainly a great abundance of quacks at this period; the line between them and the orthodox was well marked, and the College of Physicians frequently summoned the offenders before them, all too often to be flouted by the individual concerned and by his famous and grateful patients. Their efforts at thunder were softened by the knowledge that within their own ranks there were those who had devoted themselves to cults, and even such famous men as Sir Hans Sloane, Dr. Meade and Sir Charles Blicke were not above selling secret remedies. Even in the present day, quite respectable doctors have embraced cults such as Abram's Box and pendulum diagnosis. The quacks during the eighteenth century acquired more dignity than those who existed in the seventeenth century, but they never formed an organization, because they lacked sufficient cohesion. They often received Royal approval and one of their number was even honored with a knighthood. This was William Read, an oculist to Queen Anne, and it remained for another 200 years before the next quack in the person of Sir Herbert Barker was knighted in the reign of George V. The study of quacks and medical scandals of the time often help us in getting a new view upon John Hunter and his times.

When John Hunter first arrived in London, the echoes of the amazing case of the "rabbit woman" were still in the air. She was a certain Mary Tofts of Godliman, near Guildford, and the news suddenly burst upon the London world when her obstetrician, Dr. Howard, announced that after 15 labors, she had been delivered of 15 rabbits. Posthaste from London, came the King's surgeons, German, French and English, to verify this supernatural phenomenon and witness the birth of the sixteenth rabbit. This they did to their complete satisfaction and posted back to London, with the rabbit preserved in spirit in their saddlebags. Sleeping the night at Cobham, they arrived in London the next day at 10 o'clock. They then dissected the rabbit's remains in front of the King and submitted the tissues to certain tests, and, without any shadow of doubt, proved that the specimen was nothing else but real rabbit. The lady in question was brought to London, and she was kept in Lacy's bagnio in Leicester Fields, and all society crowded round the doors in the hope of getting a glimpse of Mary Tofts. The specially privileged were admitted into her room and were able to speak to her. While she was a prisoner in the bagnio, she tried to secure a rabbit by bribing the porter, and, following this disclosure, one of his Majesty's magistrates threatened her with a cesarean section unless she confessed the whole truth. After some hesitation, she did this and the mystery was over. The doctors concerned were pilloried unmercifully by the public, especially those who did the research to prove that the remains were those of rabbits, and, as a corollary, the claim that she had given birth to rabbits was authen-

tic. Their verbal efforts at extrication afterward make amusing reading. To a man, none of them had noticed the significance of the fact that the rabbits were not born whole but in pieces of convenient size. I am sure John Hunter would not have failed to notice this. I regret to say that Cheselden was drawn into this controversy, and Hogarth drew one of his complicated and somewhat inexplicable cartoons 40 years after the event, showing the rabbit running from the lady's skirts in church while a sermon is in progress.

To return to Sir William Read, basking in the sunshine of Royal patronage, he developed a tremendous practice. Not only did he couch cataracts, but he cut off "cancerated breasts and mortified limbs with very little effusion of blood because of his own patent styptic water." He was a large, dignified man to whom Kneller did justice; he had a very grand manner and lived in great state. He contrasted favorably with the cheap mountebanks of the previous century, with their attendant clowns and monkeys and theatrical behavior. He kept a lavish table, entertained Henley, Steele and Rowe; his plate was of gold and his hospitality of the most extravagant nature. He was always seeking lions—social "lions"—to grace his table, but he was unable to capture Dean Swift, who described him in one of his letters to Stella and mentioned that he had refused to go to his house to drink punch from golden vessels. After her husband's death, Lady Read did not retire, but continued to operate on cataracts in the same manner as her husband, and she would also apply styptic water. She was unable to regain the Royal Warrant, which passed to a certain Roger Grant. He was a tinker who had become an oculist and was almost completely uneducated. Although receiving the Royal Patent, he was not accorded a knighthood, possibly because he had not the dignity or presence of his predecessor, and because he descended to the selling of pills and plasters.

The sore eyes of Queen Anne were a great encouragement to the quack oculist, and, after Read and Grant disappeared, they were succeeded by the most famous and colorful of them all, John Taylor (1702-1772). He received no title from the Sovereign and he was

Chevalier John Taylor, the most picturesque of all the empirics, and one of the first to realize that specialism made a special appeal to the public.

oculist to two, so he styled himself the Chevalier John Taylor, Ophthalmiater, Pontifical, Imperial and Royal. He justified these latter titles by saying that he had treated Pope Benedict XIV and the Kings of Poland, Denmark and Norway and Sweden. He also obtained from Frederick the Great a letter patent to be his oculist, but as this was accompanied by an order to leave the country within six hours, it was not a great triumph and brought him little comfort. Frederick also added that if he touched the eyes of one of his subjects, he would string him up. It is hard to understand why Frederick bothered to give him a patent at all. Voltaire, who was living at Potsdam with the Emperor at this time, cynically observed that Frederick had driven from his dominions the only man in the world who could have opened his eyes.

Chevalier Taylor was the son of a chirurgeon in Norwich, and he was trained at St. Thomas's

Hospital under Cheselden, the great anatomist, surgeon and medical artist, who was incidentally an ophthalmologist and the discoverer of the operation of iridectomy. Taylor found life in Norwich as an orthodox general surgeon hard to bear, and he longed to specialize. He therefore embarked upon his amazing career of itinerant quackery at the age of 24. It was very essential for operating oculists to be mobile and freely itinerant and to refrain from revisiting previous haunts within 20 years, for fear that any of the blind victims were still alive. So for the next 45 years, he traveled the world, reaching as far as Moscow and Teheran. He became facile in languages, and his 55 books were published in many countries. At the age of 33, he was made oculist to George II, and among his illustrious patients was Gibbon, who said that he had been tortured by Sloane, Meade, Ward and Chevalier Taylor. He claimed to have operated upon Bach in his eighty-eighth year and to have restored his sight. Actually Bach became quite blind following the operation, which was done at the age of 61, and he died at the age of 65. He also claimed to have operated upon Handel, but had to admit failure, possibly because the patient lived too near home. Furthermore, it is generally stated that Handel's cataract was couched by William Bromfield on May 3, 1752. It is more likely, however, that Taylor operated also, because no case escaped operation with him, and it was unlikely that the blind Handel would not consult the oculist to the king, who had done so much for Handel. Taylor even operated on the hopeless condition of gutta serena, the blind eye of optic atrophy, with the wide, black, motionless pupil. For this he had a special gold file with which he rubbed the cornea or the sclerotic after piercing the conjunctiva.

A more bombastic individual never existed than Chevalier Taylor. Whether in his innumerable lectures or his 55 books, he affects a style grandiloquent to the point of comedy. One famous speech to the students at Oxford University started thus . . . "The Eye, most illustrious sons of the muses, most lyric Oxonians, whose fame I have heard celebrated in all parts of the world. The Eye, that most amazing, that stupendous, that comprehending, incomprehensible, but miraculous organ, the Eye is the Proteus of the passions, the herald of the mind, the interpreter of the heart, and the window of the soul. The Eye has dominion over all things, the world was made for the Eye and the Eye for the world. My subject is light, most illustrious sons of literature, intellectual light! Ah, my philosophical, metaphysical, my classical, mathematical, mechanical, my theological, my critical audience, my subject is the Eye. You are the Eye of England. England has two Eyes, Oxford and Cambridge. You are the right Eye of England, the older sister of the sciences and the first fountain of learning in all Europe. The Eye is the husband of the soul."

In his journeys, he met everyone of note in the scientific world, and he claimed as his acquaintances Boerhaave, Haller, Morgagni, Winslow, Munro, Linnaeus and, of course, the two Hunters. At the other extreme, he knew Matastasio, Jack Shepherd, Jonathan Wilde and, quite naturally, the "rabbit woman" of Guildford.

He was proud of his languages and they must have been good, but his Latin was dubious. On one occasion he is said to have conversed two hours in Latin with Dr. Johnson. The Doctor was not impressed, because, following this interview, he described him, "as the most ignorant man I ever knew, but sprightly." Furthermore, he cited Taylor as an instance of "how far impudence will carry ignorance."

In keeping with his speeches, Chevalier Taylor affected a grand style, and, at what he called the "crisis of his grandeur," he traveled with two coaches, each with six horses and 10 servants and livery. The coaches were painted over with numerous eyes and bore the motto—"Qui dat Videre dat Vivera." When he arrived in a town, he established himself in an inn, in a suite of rooms, and there was to be seen a display of all his decorations, his glittering gold instruments, his testimonials, public addresses and his Royal Letters of Patent. His lectures were illustrated by models of the eye in enamel, which he had purchased or had made during his Italian tour.

In spite of all his dishonesty, effrontery and mendacity, the Chevalier was thought by many to be a good operator, and he made some contributions to the surgery of the eye. Some credit him rather than Daviel with the operation of cataract extraction, and he was undoubtedly the first to do a tenotomy for squint. In his old age, he became blind, but he remained peripatetic to the end, and he died in one of the institutions he so often ridiculed, namely, a convent in Prague. His portrait was painted many times and he was the target for many lampoons and plays and operas. He figures prominently in Hogarth's famous caricature "The Undertakers' Arms."

Another crazy woman was Sally Mapp, the bonesetter, who created a great stir in the early days of Hunter's life in London. It is strange to think that Chevalier Taylor, with his studied elegance of phrase and his attitude of superiority, should have struck up a relation with this woman, whose appearance and language were equally vile. It is presumed that, medically, their paths did not cross and that they sent each other cases. Sally Mapp had a meteoric career, as had her sister who was the more good-looking and was the original Polly Peachum of the "Beggars' Opera," on whom the eyes of the Duke of Bolton rested too long, with the result that she became a duchess. Sally Mapp was born at Hindon, which is close to the fabulous Palace of Fonthill, built by William Beckford, the West Indian planter and famous Lord Mayor, who snubbed George III. Her father's name was Wallin; he was an itinerant bonesetter and took Sally to act as announcer at his booth at fairs and race meetings in Wiltshire. When he was missing, his daughter carried on and dealt with the cases, and, with her strong hands, she did even better than her father. Accordingly, she soon left him and established her own practice under the banner of "Cracked Sally—the One and Only Bonesetter." Success brought her to London; she took a house at Epsom and did much work there with the racing fraternity. While there she met and married a footman called Hill Mapp, but he soon decamped with some of her money.

Like Chevalier Taylor, she drove in magnificent state. Her coach and six horses, with footmen and outriders, was festooned with the abandoned crutches of her cured patients. She came once a week to London, where she made straightway for the Grecian Coffee House, where she consulted and saw numerous cases. This coffee house was also used by Sir Hans Sloane for his private practice and prescribing. She did a roaring trade; poems and couplets about her abounded, and a play called "Husband's Relief" concerned her. There was a Mrs. Mapp Plate at Epsom Races, and a race horse was named Sally Mapp. On one occasion, when driving up the Old Kent Road, she was mistaken by the mob in her magnificent equipage for George II's unpopular Dutch mistress (Lady Yarmouth). When held up by the mob, she put her head out of the carriage in the manner of Nell Gwynne and announced with an accent far from foreign . . . "Damn your blood, don't you know me? I am Mrs. Mapp, the bonesetter." She saw many famous patients, even the niece of Sir Hans Sloane was brought to her, and, as a consequence of this, Hans Sloane was one who championed her cause. She did so well that Chevalier Taylor and Ward parted company from her, and they tried in a court of law to obtain an injunction to stop her encouraging the singing of a couplet which ran thus . . .

> Forgot in the bustle are Taylor and Ward
> For Mapp's all the cry and her fame's on record.

Sally's retort to this threat was to encourage another couplet, viz. . . .

> Quacks without art either blind or kill
> But demonstrations prove that mine be all skill.

An affinity for alcohol ruined her career, and the coach and horses no longer clattered up the Epsom Road; she grew fatter and more loathsome and was swallowed up by Seven Dials and found her way from there to a pauper's grave.

In the cartoon by Hogarth, a gentleman with a birthmark on the left side of his face is shown resting on her shoulder. This is Joshua Ward, another leading quack of the period. He is again a strange partner for such a lady, because he came of a good Yorkshire family.

Hogarth's cartoon, "The Consultation of Physicians" or "The Undertakers' Arms." The upper three are Chevalier Taylor, Sally Mapp and "Spot" Ward, with the birthmark on the wrong side of his face. The other figures were lesser-known individuals of the period. In the middle of the second row is Misaubin, who, although qualified, came to be regarded as a quack and is one of the four doctors mentioned by Fielding in "Tom Jones."

He started life as a drysalter with his brother in Lower Thames Street, and the business premises were burnt down, Ward and a friend escaping in night attire by climbing over the adjoining roofs. From drysalting to politics was an easy step, and he was returned as Member of Parliament for Marlborough; but he only sat in the house for five months, as it was found that his election was illegal and he was unseated. In point of fact, he did not receive a single vote.

He was soon entangled in further scandal concerned with the South Sea Bubble and took refuge in France, where he started the practice of quackery with the British Colony in that country, especially in Dunkirk. His main interest was in the sale of pills and drops. In 1733, George II pardoned him and he returned to England and commenced practice immediately. His many distinguished patients included Horace Walpole, Chesterfield, Gibbon, General Churchill and Henry Fielding, who refers to him in his sad book "Voyage to Lisbon." He secured Royal Patronage and his interview with George II was illuminating. The King had a swollen thumb, which had been diagnosed as gout and which had resisted the attention of all the Royal physicians. As it happened, it was not gout but a very painful dislocation. Ward, before entering his presence, concealed in the palm of his hand some of the "Headache Essence," which, incidentally, was the original of the compound camphor liniment used even to the present day. He asked the King to be allowed to examine the thumb, and, without much ado, he seized it roughly and gave it a mighty wrench which gave the King exquisite pain; recovering, the King cursed him for a rascal in German and such English as he could muster and kicked Ward violently and petulantly on the shins. When he had cooled off, Ward asked him to move his thumb; to the King's amazement, he did it quite painlessly. Overjoyed, the King then completely changed his attitude, embraced Ward, called him his Aes-

An allegorical picture of Joshua Ward. He is seen refusing a purse of gold from Britannia and asking her to give it to the mother who is suckling her child. Various maladies can be recognized among the group of poor who importune him for help, especially the dropsical man who supports his ascitic abdomen.

culapius and asked him to take a seat. Then he asked him to name any wish in the world, and Ward modestly said that he would not like anything for himself, but could his nephew, William Gansell of Peterborough, be given a commission in the Guards. This Gansell later became a general and gave his name to the Gansell pear. When the King importuned him to take a favor for himself, he humbly asked permission to drive his carriage through St. James's Park. This apparently was a very great privilege, similar to that of driving past the Soviet Embassy today. The King not only granted this, but presented him with a coach and six horses in order that he could do so. The King also granted him a room at the King's Almonry at Whitehall, for seeing his poor patients.

Ward also took some houses quite close to Buckingham Palace, or Buckingham House as it was called in those days, and he also had a surgery for poorer people in Threadneedle Street. Pursued everywhere by a torrent of jealous criticism from the doctors and from the lay, he nevertheless flourished and his practice grew and grew. Most of his remedies contained arsenic or antimony, and, strange to say, two of his prescriptions have lived to the present day, friar's balsam and the compound camphor liniment. He was very conspicuous on account of a large port-wine stain on his face, affecting the lower two divisions of the fifth nerve on the left side. On account of this stain, he was known as "Spot" Ward, and he was recognized by all the street hawkers and crossing sweepers because of his disfigurement, which had some publicity value. He, however, was ashamed of it, although his two portraits by Loving and Bardwell show it very clearly. Unable to find an artist who would paint him without the mark, he hit upon the ingenious idea of having his statue carved in white marble. This was done by Carlini, who was paid 200 guineas a year until it was completed. Actually, he continued to receive the money until Ward's death, which was many years after the statue was completed. The statue now stands in the home of the Royal Society of Arts in the Adelphi. Appar-

Loving's portrait of Joshua Ward, showing the trigeminal nevus, which gave him his nickname of "Spot."

Plate V of the "Harlot's Progress," by Hogarth. The harlot is dying, with her finery on the clothesline and a maid rifling her trunk, while "Spot" Ward and Misaubin, well-known quacks of the period, argue on the treatment in the background.

ently, Ward played some small part in the initiation of the Royal Society of Arts. Hogarth portrayed him in "The Undertakers' Arms," as we have seen, and he is also shown in plate V of the "Harlot's Progress" in consultation with Misaubin, another less-known quack of the period. He was protected by a special decision of Parliament from being called before the Censors of the College of Physicians, and he was exempted by name (a very special concession) in the Apothecaries Act of 1748.

Queen Caroline allowed him to demonstrate some of his cures before her in Kensington Palace. Honored by the highest in the land in a very special way, he, nevertheless, did not desist from persistent bragging and continuing to be quite unscrupulous. He lived in great style, but he was kind to the poor, giving them his money, but neutralizing it by giving them his pills. Society ladies fawned upon him and helped him with his outpatients and distributed his pills and drops among the poor. When his death was nigh, he asked to be buried close to the altar rails of Westminster Abbey, but this did not eventuate, and he was buried in a more remote part of the Church, namely, the Southern Cross, where the stone marking his grave can no longer be deciphered. It may have born the epitaph—"Restorer of Health and Father of the Poor"—a title he arrogated to himself during his life. The Abbey, at the time, was open to those who lived in the parish for burial purposes, and Ward's estate paid £54 19s. 6d. for the interment. The bill is still in existence, and one notes that the hearse with six horses cost 24 shillings. So passed away this great public figure, probably known to all his contemporaries at the time, pompous and portentous, cartooned twice by Hogarth, mocked at by Pope, and cordially detested by our profession, but, nevertheless, extremely successful in his relations with the public. In achieving burial in the Abbey, he was better treated than John Hunter, who, after the humblest of funerals, remained in the crypt of St. Martins-in-the-Fields, until his body was removed 60 or more years after his death to the Abbey, and there reinterred at the expense of the Royal College of Surgeons and as a result of the labors of Buckland.

Another woman quack of this period who had great success was Joanna Stephens, who devised a remedy for stone. The possessors of stones in the bladder and kidneys were numerous in this age; the overindulgence of the gouty upper classes was often attended by this affliction. Their sufferings were terrible but, fortunately, intermittent, and they presented an easy prey to this unprincipled lady. She soon had plenty of supporters for her remedy, members of the Peerage, high dignitaries of the Church and Members of the House of Commons. Knowing the fate of Sally Mapp, it occurred to her, as her remedy was so well received, to offer it to the public for the small matter of £5000 sterling. A subscription list was opened at Drummonds Bank, but her right friends in the Church, Peerage and Parliament, only raised £1,356. She then took the matter up in Parliament, and if the public of England was not gullible enough to find the £5000, their representatives in Parliament were; but then as now it was not their own money. A suitable committee was formed, consisting mainly of subscribers to the fund in Drummonds Bank, but I am sorry to say that three of the leading surgeons of the day, Cheselden, Caesar Hawkins and Sharpe, joined the committee; apparently, there is nothing that the profession will not do for the govern-

ment. Included in the committee was also that remarkable individual, the scientific researcher who was the Vicar of Teddington, Stephen Hales. After investigating the remedy, seeing the patients and stones they had passed, this committee reported favorably upon it; Parliament found £5000 and the secret was revealed. The main constituents were egg shells, snail shells and soap. One could not imagine a worse possible medicine for stone in the renal tract. The amount of soap consumed was prodigious, even as much as 4 oz. a day, quite sufficient to make the patient foam at the mouth. Sir Robert Walpole, who was a devotee of Joanna Stephens, during his lifetime consumed nearly 2 cwt. of soap and the equivalent of 1200 gal. of limewater, and at his postmortem, Ranby and Caesar Hawkins, who had been on the committee of investigation, found three large stones in his bladder. His brother, Sir Horace, said that he had been killed by a lithontriptic medicine from a quack. This extraordinary behavior of Parliament has often been repeated. In recent years, one can recall the Hong Kong Legislative Council with a cure for sprue, Lloyd George's government with a wart charmer, Mr. Baldwin's government with Spahlinger's cure for tuberculosis, and, most recently of all, Mr. Aneurin Bevan, who appointed a commission, including Sir Alexander Fleming and Sir Ernest Rock Carling, to enquire into the remedy of a cancer quack who had been practicing for many years. One can also call to mind a committee of investigation appointed with Lord Horder as chairman to enquire into Abram's Box, which reported that there might be something in it! As with all these other remedies, as soon as they were paid for and the secret disclosed, Joanna Stephens' egg shells, snail shells and soap, very quickly went out of fashion.

A very theatrical person in the middle part of the eighteenth century was Martin Van Butchell, who claimed to be a student of John Hunter's. He was a born advertiser; without a trace of self-consciousness, he affected a long beard and rode a white pony in the park and to his place of work in Mount Street, carrying, as he rode, a stick made of human bone. The pony was painted differently each day, sometimes with large purple spots; sometimes, it was painted all over a bright purple. At first he was a simple quack, selling nostrums and claiming to cure anal fistulas, but later specialized in dentistry and especially upon dentures, which he fitted over the undrawn stumps. His wife's death in 1775 was a great blow to him, and he asked William Hunter and Cruikshank to embalm her. They removed the viscera and packed the abdominal cavity with camphor and injected the circulation with turpentine and a solution of camphor in spirit. In a coffin with a glass lid, she was kept in his waiting room, and her complexion was very lifelike, because of William Hunter's injections of carmine and various stuffings in the cheeks and the fitting of a pair of glass

The picturesque quack who divided his attentions between artificial dentures and fistula in ano. The painted horse and peculiar attire were to attract attention, as was the embalmed body of his wife, which he kept in his waiting room.

"Doctor" Bossi, an old-fashioned quack, and his zany hawking his medicine in Covent Garden. His methods were those of the seventeenth century.

eyes. An epitaph on the coffin read . . .

Here entombed Van Butchell's consort lies;
To feed her husband's grief or charm his eyes.
Taintless and pure, her body still remains
And all its former elegance retains.

William Brodum, who made sexual psychosis his specialty and used the title, M.D., Aberdeen. His cordial was the antecedent of the "nerve tonics" of the present day. He was previously footman to Bossi.

Long had disease been preying on her charms
Till slow she shrank in Death's expecting arms.
When Hunter's skill in spite of Nature's laws;
Bade the pale roses of her cheeks revive
And her shrunk features seem again to live.
Hunter who at first conceived the happy thought
And here at length the full perspection wrought.
O lucky husband, blest of Heaven;
To thou a pleasure it is given.
A much loved wife at home to keep;
Caress, touch, talk to, even sleep,
Close at her side when ere you will:
As quiet as if living still.
Strange to tell that fair is she
And sweeter than alive should be.
Where plump and juicy as before
And full as tractable or more.
Thrice happy mortal, envied lot,
Rich treasure has thou got.
Who to a woman can lay claim;
Whose temper's every day the same.

When Van Butchell, some years later, again launched his vessel on the seas of matrimony, his new-found bride found the late wife a source of great humiliation, and the corpse found its way into the collection of John Hunter, and thence to the curio room in the College of Surgeons, where it was exhibited standing up, together with Van Butchell's peculiar walking stick. The body was eventually cremated on May 11, 1940, as the result of an air raid, and one of the strangest methods of advertising disappeared forever.

Lesser lights among the quacks at this time were a group of Germans: Bossi, Brodum, Solomon and Katterfelto. Dr. Bossi was one of the older school, who practiced on an open-air stage in Covent Garden. He was assisted by a harlequin clown and a blasphemous parrot, and he had that invaluable asset to a successful practice in this country, namely, a very strong foreign accent. His footman, Brodum, put up a brass plate on his house in Grosvenor Square, calling himself Dr. Brodum. On this account, he was called before the President and Censors of the College of Physicians and told to take down the plate and to cease taking fees. He refused to do this, saying that he had bought his degree quite legitimately in Aberdeen. He specialized in the psychologic repercussions of sex, treating them with a "nervous cordial" and a "botanical syrup."

Dr. Solomon practiced in the Midlands; he made a great mystery of his medicines, which

Doctor Katterfelto, who may have antedated Koch and Pasteur in the microbic causation of disease.

were made from gold and the Balm of Gilead. He carried a very imposing gold-headed cane to indicate that all his medicines contained gold. Madame Tussaud, who was just starting her collection, wished to include him in her waxworks, and, unfortunately, in taking his facial impression, she omitted the hollow reeds which are usually stuck in the nostrils and nearly suffocated him. Too frightened for a repetition, he never appeared in her collection. He, like many another quack, affected a great style, coach and horses, magnificent house; and he entertained sumptuously. He was waylaid by some practical jokers in a country lane and made to consume a large volume of his balm of gold, without doing himself any harm. Consequent upon this attack and the ridicule that arose from it, he left Liverpool and started to work in Birmingham. On his death, he was buried in the front garden of his own house.

Dr. Katterfelto, another of this small group, thrived on the great influenza epidemic of 1782. He sold a medicine known as Dr. Bato's Medicine. He made himself conspicuous by driving in a large caravan with numberless black cats to match the first syllable of his name. He also gave scientific exhibitions in which he displayed insects by means of an instrument called the solar microscope. With this he demonstrated on a screen the insects which caused the recent influenza. He said that they would show as large as birds. He demonstrated the insects in a drop of pond water; he showed them from milk, vinegar, flour, blood, cheese and vegetables. Following on his lecture, he gave instructions in cards, dice, billiards and E.O. tables. He was doing very well, when he suddenly disappeared, saying that he had been called up to take his commission by the Emperor of Prussia in the Death's Head Hussars.

Toward the end of John Hunter's life, America began to make itself felt in the field of quackery, a foreign export which she has maintained to the present day. About this

A poor drawing of "Doctor" James Graham giving one of his famous health lectures, which were a source of considerable revenue to him. He employed Emma Hamilton as a model to illustrate his points.

time, Benjamin Franklin's electrical discoveries were causing a great stir, and the two quacks who came across to us from America were greatly influenced by him. They were James Graham and Elijah Perkins.

James Graham was born in 1745 in Edinburgh; he was the son of a saddler. He became a student in the School of Medicine in Edinburgh, which Dr. Cullen had recently started, and he studied under him and Munro. These two individuals had a considerable controversy with John Hunter. James Graham emigrated at the age of 26 to America, and he returned to England three years later, at first practicing as an eye, ear and nose specialist in Bath. He then came to London, where he practiced, and in Paris. He soon had famous patients, among them were Catherine Macaulay and the great Georgiana, Duchess of Devonshire and Lord and Lady Spencer. With the patronage of these people, he soon became widely known, and with his ambition fired by his social contacts, he opened a palatial establishment in the Adelphi. It was called the Temple of Health and dedicated to the god Apollo. Inside, the display of brass and glass and scientific apparatus was awe-inspiring. Electricity and magnetism were largely featured as a result of his connection with Benjamin Franklin. The *pièce de résistance* was his celestial bed made by a great craftsman, Denton; it was said to have cost £10,000. The bed contained three-quarters of a ton of compound magnets, continually pouring out magnetism in an ever-flowing circle, and concealed lights glittered, and instruments played romantic tunes, and tubes exhaled all the stimulating perfumes of the Orient. His idea of the bed was to combat sterility and to ensure that children of the most perfect beauty could be begotten as a result of the magnetic waves, which were the feature of the bed.

Graham endeavored to secure the services of O'Byrne, the Irish giant, for the opening ceremony of the bed, but the giant did not rise to the occasion, and endocrinologists will doubtless understand his reluctance. The fee for the lease of the bed for one night was 500 guineas; to John Hunter this must have seemed a lot of "guid siller." It will be recalled that, at a later date, John Hunter secured the skeleton of this giant for his museum, and it can be now seen in the College of Surgeons. Graham made his money by the fees for this bed, by fees for prescriptions, by means of a magnetic crown, lowered over the head, and by an electric chair. He also gave lectures, with seats from five shillings to one shilling, and there came sometimes as many as a thousand to listen to the atrocious nonsense which he poured out. Underneath this nonsense, ran an undercurrent of eroticism. The lecture was interspersed with recitations and choruses from unseen voices and music by a hidden orchestra. The crowning point was reached when a previously curtained alcove opened and exposed completely unveiled the rosy Goddess of Health, who was none other than Emma Lyon, later to become Lady Hamilton, the companion and comforter to Lord Nelson of the Nile. After an uproarious success, Graham took larger premises, Schomberg House in Pall Mall, but the pace was too fast; the new and better celestial bed was only new, and, chased by creditors, he faded away into a peripatetic existence in the provinces. Later, religion and eugenics obsessed him; he became addicted to ether and had a psychosis resembling general paralysis of the insane. He passed away in Edinburgh, the town of his birth, at the age of 49. He will probably be remembered as the outstanding quack of all times; the liberties he took with human credulity will never be excelled.

He was followed by another American, Elijah Perkins, who devised his electric tractors which were made of brass and iron, which drew the disease out of the affected organ, when it was stroked in a downward direction. George Washington bought a set for the use of himself and his family, and the American public followed dutifully in his trail. When the novelty died away in America, his son brought them to England, and, strange to relate, he took over John Hunter's old house in Jermyn Street. The electric tractors were five guineas a pair; the Royal society was impressed and accepted a pair, and a Perkins Institute was started where the poor were treated by means of the tractors. The tractors

Gillray's cartoon of the drunkard's nose being treated by Perkin's electric tractors.

were mentioned by Byron in his satire . . . "English Bards and Scottish Reviewers," and Gillray made an amusing cartoon showing their use in rhinophyma. The vogue was exposed by Dr. Haycraft of Bath, who made imitations in wood which were so successful as almost to draw Haycraft into the vortex of empiricism. Perkins, after this, packed his bags, forgetting the unsold tractors, and sailed back to America, counting his profits and, I am certain, laughing heartily over human simplicity.

There were other practitioners of this amusing profession such as Loutherborough, a good painter and a member of the Royal Academy. He practiced his occult medicine in Chiswick, and he really believed in himself; because of this his skin was too thin and he lacked the ruggedness of Sally Mapp, for, after being roughly handled by the crowd outside his Chiswick house, who were exhorted to do so by a disappointed patient, he dropped out and disappeared, it is thought to Switzerland, where he and his wife joined Cagliostro, an Italian healer, who was also in decline.

Mr. Patence was a dancing master, who combined this with quackery; he is said to have originated the expression "worth a guinea a box." Naïvely, he states in his pamphlet the following . . . "To show its safety, sovereignty and efficacity, either when in health or sickness, Mr. Patence constantly takes his own pills to preserve his own health." It is impossible to think of anything fairer than that.

As the century was drawing to a close, the birth of the patent medicine was manifest; quacks, reveling in their powers, began to specialize on one nostrum, and Nathaniel Godbold, a gingerbread baker, made a large fortune from his vegetable balsam. His house at Godalming cost £30,000, and his gravestone in Godalming churchyard is nothing more or less than an advertisement for his balsam.

Swainson was another in Twickenham, who made Velno's vegetable syrup for lung conditions. He lived in a large domain in that place and developed a remarkably good botanical garden. These men showed the way to Holloway, Owbridge, Carter, Beecham, Sloane and many yet to be born.

John Hunter never showed any great animosity toward these people; many claimed

Nathaniel Godbold, the pioneer patent medicine vendor, who made a large fortune out of his vegetable balsam for consumptives. He was probably the first to realize the possibilities of a widely advertised and distributed patent medicine.

him as tutor and acquaintance, and one secured the good offices of his brother in order to convert a wife from a corpse to a means of publicity. Possibly, Hunter had a little fellow feeling for the quacks, because his great critic and opponent, Jesse Foot, would, when not reviling Hunter, pour stinging invectives on the quacks, both generally and individually. If Hunter returned today, he would perhaps justify his tolerance and say that Sally Mapp was a pioneer of orthopedics; Chevalier Taylor showed the way to lens extraction and tenotomy for squint; "Spot" Ward blazed the trail which led to arsenobenzol and thence to modern chemotherapy. Katterfelto was a forerunner of Pasteur and Koch, and even Graham had his niche in the annals of medicine by originating the specialty of electrotherapy, which would later provide a living for 150 physiotherapeutic specialists and thousands of their acolytes, who serve in our Health Service.

Epilogue

In bringing this oration to an end, I would like to say that in the heart of this Society you, John Hunter, live on. Everard Home may have tried to destroy your memory in the holocaust of Earl's Court, but we snatch up greedily every scrap that he left unburnt. Our Society will go on through ages to come, with your example to inspire us. Yearly orators will continue to burn the midnight oil in preparing the studies of your life and times and take a joy in keeping your memory green. Hard-working officers, such as those we have now, will forever strive to keep the Hunterian tradition alive. How would we as a Society have fared if that rather pompous pupil of yours, Sir William Blizard, had had his way and called this Society by another name?

MEETINGS *and Postgraduate Courses*

AMERICAN ACADEMY OF FORENSIC SCIENCES, CLEVELAND: Annual meeting, February 27-March 1 at the Carter Hotel. The tentative program includes a review of what's new in forensic sciences; sectional meetings in pathology, toxicology, jurisprudence, questioned documents, immunology and psychiatry; and a symposium on investigation of sudden, unexplained or obscured deaths. The banquet will be on February 28.

AMERICAN COLLEGE OF SURGEONS, CHICAGO: Postgraduate course in fractures and other trauma to be offered by the Chicago Committee on Trauma, April 16-19, at the John B. Murphy Memorial Auditorium, 40 East Erie Street. For additional information, write to: Dr. John J. Fahey, 1791 West Howard Street, Chicago 26.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION, NEW YORK: Three day annual meeting, beginning March 6 at the Commodore and Roosevelt hotels. Emphasis will be on research and public health aspects of mental health. For further information, write to: Dr. Marion F. Langer, Executive Secretary, American Orthopsychiatric Association, 1790 Broadway, New York 19.

STATE UNIVERSITY OF IOWA COLLEGE OF MEDICINE, IOWA CITY: Postgraduate course in anesthesia, March 18 and 19. For further information, write to: Dr. W. C. Keettel, Postgraduate Medical Studies, Office of the Dean, College of Medicine, Iowa City.

UNIVERSITY OF MINNESOTA, MINNEAPOLIS: Courses to be presented at the Center for Continuation Study:
Pediatrics for general physicians, March 3-5
Internal medicine for internists, March 17-19
Surgery for surgeons, March 20-22
Radiology for general physicians, April 7-9
For further information, write to: Director, Department of Continuation Medical Education, 1342 Mayo Memorial Building, University of Minnesota, Minneapolis 14.

UNIVERSITY OF OKLAHOMA MEDICAL CENTER, OKLAHOMA CITY: Postgraduate courses for 1958:
Basic electrocardiography, March 31-April 5
Trauma, April 11-12
Oklahoma House Staff Physicians Association, May 23
For further information, write to: The Office of Postgraduate Education, University of Oklahoma Medical Center, 801 N.E. 13th Street, Oklahoma City.

WESTERN RESERVE UNIVERSITY LAW-MEDICINE CENTER, CLEVELAND: The fourth in a series of institutes will be held April 25-26 in the courtroom of the University's School of Law. The program is entitled "The mind: A law-medicine problem." For further information, write to: Oliver C. Schroeder, Jr., Director, Law-Medicine Center, Western Reserve University, Cleveland 6.

Editorials

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TAX EQUITY FOR DISABLED*

Two tax rulings were given toward the end of 1957 which affect a substantial number of patients of most practicing physicians.

The first was the denial by the Federal Tax Court of a claim for the deduction of expenses for a specially equipped automobile used by a man paralyzed from polio in traveling to and from work. The second was a ruling by the Internal Revenue Service that the expenses of caring for a Seeing Eye dog, even when it is used in the conduct of business, may not be deducted.

In the first case, the man had claimed a deduction of $1800 for his automobile, which is equipped with hand controls, for expenses "essential to production of income." The court, however, ruled that despite his disability, "his expenses related to that automobile are, in essence, nothing more than a commuter's expenses, which are personal in nature, and, therefore, specifically not deductible."

In its ruling on the Seeing Eye dog, the Internal Revenue Service quoted a similar situation in which deduction was not permitted for the cost of maintaining a hearing aid as a business expense even though the taxpayer was a lawyer. It did rule, however, that the expenses of caring for a Seeing Eye dog might be deducted as a medical expense rather than as a business expense.

But the catch here is that, whereas business expenses are totally deductible, only that portion of medical and dental expenses that exceeds 3 per cent of adjusted gross income is deductible.

For a number of years, various organizations have sought legislation providing tax relief for certain other disabled individuals, such as the annual exemption of $600 allowed the blind.

A bill to provide such relief is now before the House of Representatives. It was introduced by Representative Eugene J. Keogh, Democrat of Brooklyn, and bears the endorsement of a great many veteran, fraternal and labor organizations. It would provide a disabled individual with an additional tax exemption of $600 annually and an additional $600 exemption for his spouse, and would include transportation costs to and from work by disabled persons as tax-deductible business expenses. A similar bill introduced by Congress-

*Adapted from an article which appeared in *The New York Times.*

man A. S. Herlong, Democrat of Florida, goes somewhat further and proposes, in addition to an exemption for the disabled taxpayer and spouse, an additional exemption to a taxpayer who is supporting a dependent who is permanently disabled.

It would seem that there could be no argument against the provision of these proposals which would include transportation costs to and from work by disabled persons as tax-deductible business expenses. Persons with physical disabilities practically always have extraordinary expenses in connection with the production of income. Many cannot use public transportation and must use taxicabs or have specially equipped automobiles. The recent case of the expenses in using the Seeing Eye dog and the prior ruling on hearing-aid maintenance for a lawyer are other examples.

To make these expenses tax deductible would be entirely consistent with basic income tax principles. These permit other categories of wage earners to deduct certain expenses that they incur as a necessary part of their income-producing activities. This situation would be no different from that of the salesman who deducts entertainment expenses or the physician who deducts the cost of operating his car on professional calls.

There is also little doubt that such a ruling would motivate certain disabled persons to seek employment. This writer knows personally of numerous instances in which disabled persons, having been placed in employment after rehabilitation, actually have less net income after their travel costs to and from employment than when they received public assistance prior to rehabilitation. It is difficult to motivate a person to work if by so doing he loses money.

The other provision of the Keogh bill—the annual exemption of $600 each for the disabled person and his spouse—is designed to aid those with extraordinary expenses that are incurred because of disability but that are not related to the production of income. The Herlong bill would add to the provision for the disabled taxpayer and spouse an additional exemption for dependents who are permanently disabled.

For example, not all costs incurred in the purchase and maintenance of orthopedic and prosthetic devices are completely deductible under the medical deduction provisions of the law. Wheel chairs used by active disabled persons require repairs and maintenance. Many disabled persons require custom-made clothing or alterations on clothing. Clothing of persons using orthopedic and prosthetic appliances is subjected to unusual wear.

Some disabled persons must, of necessity, live in ground-floor apartments, which command higher rentals. Others must invest in ramps and special household equipment. The severely disabled person cannot climb to the balcony; he must pay the higher cost of orchestra seats at the theater or a concert.

These are little things. But they loom large in the budget of disabled persons when they come up 365 days a year.

The proposed additional $600 exemption for the physically disabled would be more difficult to administer than that which now exists for the blind. In the case of blindness, there are accurate measurements to determine if an individual is "legally blind." There are, however, no similar easily applied, objective yardsticks to measure functional capacity in other types of disabling conditions. This must be based on the clinical opinion of a physician. Admittedly, there might be some abuses of the proposal, but evidently the Medical Society of the State of New York thinks these would be minimal, for it has endorsed Mr. Keogh's bill. In any event, the moral and practical values would far outweigh possible limited abuses.

The "treatment" the physically handicapped ask is not favoritism or "special treatment." All they want is equity and parity.

HOWARD A. RUSK

THE VOLUNTEERS

A NEW book by David L. Sills* of the Bureau of Applied Social Research of Columbia University analyzes the organization and method

*SILLS, D. L.: The Volunteers; Means and Ends in a National Organization. Glencoe, Illinois, The Free Press, 1957. $6.00.

of functioning of the National Foundation for Infantile Paralysis. This Foundation was selected for the study on the grounds that it constitutes the largest volunteer health organization in the United States, and because it is today at what might well be a termination of its primary interest in infantile paralysis and the beginning of a new life. Because of federated fund raising and the creation of such organizations as the United Fund and the Community Chest, the whole question of the organization and support of volunteer agencies, particularly in the field of health, is today prominently before the American people. The leaders in the group, such as the National Foundation for Infantile Paralysis, the American Heart Association, the American Cancer Society, the National Society for Crippled Children and Adults, and the National Tuberculosis Association, have not affiliated themselves with the federated fund-raising activities. However, the Red Cross, with many branches throughout the nation, recently joined with these federated fund-raising groups. In many cities the number of organizations involved in a united fund may be well over 100 and in some instances the number may approach 200. The arguments against this procedure center around the concept that the giver should have a knowledge of the philanthropy to which he is devoting his funds. Giving should be intelligent and not automatic; the deduction of a certain percentage from the wages of an individual to be contributed to all charities of a community becomes essentially a tax rather than a contribution. On the opposite side are the arguments that people are being beseiged by far too many organizations, that giving becomes a nuisance instead of a charity, and that industries do not wish to be called on to devote their internal organizations to fund raising for any considerable length of time. Most of the months of the year are now devoted to special causes, such as January for infantile paralysis, February for the heart diseases, March for the crippled, April for cancer, and so on up to November and December for tuberculosis. The decision is not yet crystallized in public opinion and will probably not be crystallized until far more information has been assembled as to just what the philanthropic funds represent in our social scheme.

David L. Sills' book is the most comprehensive and scientific study of a foundation yet attempted. Incidentally, attention is called to the fact that the great Alexis de Tocqueville found more than a century ago that ". . . in no country of the world has the principle of association been more successfully used or applied to a greater multitude of objects than in America." And that observation is far more true of conditions that prevail today than it was when de Tocqueville wrote it.

The chief concern of the book is the process through which the members of a voluntary association helped to shape the organization's character and to determine its future. The author finds that the Foundation has been extremely successful in maintaining a high level of interest among its members, in achieving its major goals, and in avoiding the organizational frustration which is so characteristic of voluntary associations.

As already announced, the decision by the National Foundation for Infantile Paralysis concerning its plans for the future has not yet been made, principally because the program against poliomyelitis continues to present unfulfilled needs. Thousands of those who have had the disease still need medical and financial assistance. As was stated in an editorial in POSTGRADUATE MEDICINE recently, the number of persons requiring rehabilitation approximates 300,000. Moreover, our public has not been fully protected with the three necessary injections of the Salk vaccine, and the question arises as to how great a saturation of vaccination needs to be achieved to control the disease as typhoid fever and diphtheria have been controlled. Certainly in the not too distant future, the Foundation will have to develop new goals if it is to continue to expect support from the public and from its own volunteers. Mr. Sills points to the many goals to which the Foundation has made significant contributions in areas related to infantile paralysis. Research has been concerned with the possibility of vaccines against other viruses that affect the nervous system. Medical schools have been aided in developing new programs

of professional education. Improved methods have been evolved for assisting in the physical, social and vocational adjustments of disabled persons. In fact, the Foundation has led many of its own volunteers to perceive the organization as a social movement and has thus provided them with an ideologic rationale for participation in the future. The final statement of Mr. Sills reads:

"The very existence of these perceptions is thus a strong indication that the activities of volunteers have been more than a campaign against polio, more than a means to an end, and more than the pursuit of a realizable goal: they have in themselves been instrumental in bringing other ends in view."

MORRIS FISHBEIN

HOSPITALS, PUBLIC RELATIONS AND CHEERFULNESS

THE Louis A. Weiss Memorial Hospital in Chicago takes its public relations seriously—so seriously, in fact, that a public relations agency is regularly employed. The executive director of the hospital, working with the public relations agency, has developed some ideas which seem to have aroused enthusiasm in the clientele. Gay colors have been used in the furnishings and decoration. Maternity rooms are pink and white. Any patient may talk over the patient-to-nurse speaker to the nursing station. Metal plates keep the food hot. Patients receive free newspapers. A special room has been arranged for expectant fathers. The hospital, like all newer hospitals, is equipped with a recovery room. Educational activities include extern and resident training and, particularly, general practice training at the residency level. Patients who come for operations receive a card which informs them that they are to become members of the "Did I Tell You About My Operation Club?" and lists five statements concerning some of the benefits:

1. You will receive dinner about 5 P.M. the night before your operation.
2. Enemas may be ordered following evening meal. Skin area around the area to be operated on will be shaved. This will be done the evening before surgery. However, in some cases it may be done in the morning before surgery.
3. A sleeping pill may be ordered for you in the evening, if you need it.
4. You will not eat or take anything by mouth after 12:00 P.M., if you are scheduled for surgery the following morning.
5. Ladies! The nurse will ask you to remove your nail polish, jewelry, hairpins and make-up.

In addition, six cards have been developed which describe the routine in detail for various types of laboratory procedures, so that patient cooperation is secured in the taking of specimens.

As one who has undergone operation and who has observed the varying procedures in hospitals throughout the United States, I would enthusiastically endorse this progress in patient-doctor-hospital relationships.

MORRIS FISHBEIN

AMYOTROPHIC LATERAL SCLEROSIS

AMONG the unsolved problems of medical science is a disease characterized by atrophy of the muscles and sclerosis of the lateral columns of the spinal cord, as indicated by its name, amyotrophic lateral sclerosis. During a symposium[1] at the Mayo Clinic, Eaton reported that each week about two patients with this disease come to the clinic, making 100 new cases annually, an incidence which is twice as great as that of myasthenia gravis and one-third that of multiple sclerosis. The condition, commonly called Lou Gehrig's disease because it was that from which the celebrated baseball player died, is almost invariably fatal.

Mulder reviewed the clinical signs in 62 patients with this disease whom he examined in the Mariana Islands and in 100 patients seen at the Mayo Clinic. From this tremendous experience, which is far beyond that which could come to any individual physician elsewhere, he has developed a description which is most informative. Classically, the ill-

ness begins with weakness in the small muscles of the hand. The weakness and atrophy begin unilaterally and remain so for several months or occasionally for as long as a year. Then the disease spreads to similar involvement of the opposite hand. With the weakness, loss of muscle substance and of subcutaneous fat occurs and the hand assumes a cadaveric appearance. Other musculature becomes involved. The initial symptom of many patients is muscular cramping which is commonly found in muscles already weak. Less frequent as a site of onset is the shoulder girdle, with weakness beginning on one side in either the deltoid or the scapular muscles. In women the subcutaneous fat may for a time conceal atrophy and weakness about the shoulder. In a large percentage of patients weakness began in the lower extremities involving the tibial and gastrocnemius muscles with development of a flail foot.

In about one-fourth of the cases of amyotrophic lateral sclerosis in these two series, the original presenting complaint involved bulbar symptoms. The patient complained of difficulty in moving his tongue which resulted in mushy speech, and difficulty in holding food in the mouth. The tongue was atrophic and the lips were weak. Later came weakness of the pharyngeal muscles and the vocal cords with accompanying difficulty in swallowing and talking. Because of the difficulty in moving food in the mouth, spoon feeding was tried with the food placed in the posterior pharynx. The progression of the disease was constant, with death resulting from aspiration pneumonia or mechanical failure of respiration. In a few instances the patients described the muscular atrophy as beginning in the trunk or in the neck.

With involvement of the lateral or pyramidal columns of the spinal cord, reflexes became hyperactive, spasticity occurred, and occasionally there were abnormal plantar responses. Involvement of the pyramidal tracts above the level of the brain stem brought about hyperactive jaw jerk, a sucking reflex and emotional incontinence. The sensory symptoms were mainly concerned with the muscle cramping and pain but there were, of course, other involvements. In many older patients a diminution of vibratory sensation in the legs was observed.

Summarizing his observations, Dr. Mulder states:

> The patient, usually a man in his forties or fifties, presents a clinical picture of widespread asymmetric steadily progressive muscular weakness with atrophy and fasciculations and associated hyperreflexia and spasticity in the remaining musculature. Involvement of the muscles controlling eye movements does not occur, and impairment of bladder sphincters is infrequent. Although cramping muscular pains are a frequent complaint, objective sensory impairment is not a part of the clinical picture. The electromyogram is usually sufficient in such a patient to confirm diagnosis.

Dr. Mulder has a few paragraphs on treatment, which unfortunately is not at all specific, involving merely the avoidance of fatigue and the use of strengthening exercises, the maintenance of adequate nutrition, and emergency tracheotomy or gastrotomy when needed. In a few patients PROSTIGMIN® in small doses has seemed helpful. The Mayo Clinic has tried all of the various treatments reported in medical literature, including vitamins, hormones and calcium disodium versenate, but the results have been monotonously unsatisfactory except for psychologic effects.

Since the cause of this disease is unknown, any hypothesis based on such a study as has been made by Dr. Mulder is worth consideration. Dr. Mulder says:

> These observations suggest that the pathophysiology for this disease may be a widespread but selective disturbance of the metabolism of the neurons of the motor system which, at least in some instances, is inherited. The local site of onset and the asymmetry of the disease could then be explained by a localized precipitating factor such as fatigue, infection, or trauma. Such a hypothesis, in which it is assumed that a selective "metabolic" defect is a necessary but not always sufficient cause of the illness and that local noxious stimuli are the precipitating causes, may be helpful in orientating further therapeutic trials and etiologic studies.

Through the National Institutes of Health, Dr. Leonard T. Kurland has made observations in Guam where a high incidence of this disease has been detected. The incidence of the disease in Guam has been estimated as about 420 per 100,000 population which is about 100 times that of the incidence in the United States. The population of Guam includes about 59,000 persons. The disease is not prevalent among other peoples of the Mariana Islands. About 10 per cent of the deaths of adults are reported due to this cause in Guam compared to a rate of 1 in 100,000 in the United States. Incidentally, this high rate also prevails among natives of Guam who have migrated to California; therefore, the condition is considered to be hereditary. In Guam there are instances of multiple cases in the same family, and Dr. Kurland is convinced that the disease among the Chamorros is of genetic origin with the condition inherited as an irregular dominant as a metabolic defect. Dr. Kurland says, "The hypothesis of an endogenous mechanism or metabolic defect responsible for amyotrophic lateral sclerosis and the likelihood of dependence of prevention and control on clarification of the abnormal chemistry of the affected motor neurons are reiterated."

In this symposium as reported from the Mayo Clinic other contributions are concerned with pulmonary disability, disturbances of esophageal motility, and electromyographic and pathologic investigations. Here then is the latest word on a condition which continues to baffle scientists. However, knowledge is being accumulated regarding this and many similar disorders. With the new devices and new technics now becoming available, hope is warranted that determination may yet be made as to means of prevention, if not successful treatment, of these desperate diseases.

MORRIS FISHBEIN

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THE USE OF BCG

Since its establishment the World Health Organization has been concentrating on the use around the world of vaccination against tuberculosis with BCG. Many millions of children have been inoculated and the safety of the method has been established. Because the use of this product has been continuously urged by some leaders in the United States, Surgeon General Leroy E. Burney appointed a committee,* headed by Dr. Esmond R. Long, to consider the possibilities of widespread inoculation; this committee has just made its report. Briefly the report recommends that BCG tuberculosis vaccine be used only in groups or communities where exposure to the disease is unusually high and where other means of control are inadequate. The committee concluded that the use of the vaccine should be limited to physicians and other medical personnel working in hospitals without adequate programs for the control of tuberculosis, families in which one person with tuberculosis must remain at home, and persons associated with institutions in which exposure is known to be high, such as certain mental hospitals and prisons. The committee pointed out that BCG does not offer protection to persons who are already infected and who are most likely to

*The committee is composed of Dr. Esmond R. Long, chairman, retired medical director, Henry Phipps Institute, Conifer, Pedlar Mills, Virginia; Dr. Rene Dubos, Rockefeller Institute for Medical Research, New York; Dr. Herman Hilleboe, commissioner of health, New York State Department of Health, Albany; Dr. Horace L. Hodes, clinical professor, Columbia University, chief, pediatric service, Mt. Sinai Hospital, New York; Dr. Walsh McDermott, editor, *The American Review of Tuberculosis and Pulmonary Diseases,* New York; Dr. Gardner Middlebrook, director of research, National Jewish Hospital, Denver; Dr. Rufus F. Payne, director, Eugene Talmadge Memorial Hospital, Augusta, Georgia; Dr. James E. Perkins, managing director, National Tuberculosis Association, New York; Dr. Leon H. Schmidt, director, Christ Hospital Institute for Medical Research, Cincinnati; Dr. Jacob Yerushalmy, professor of biostatistics, University of California School of Public Health, Berkeley.

develop active tuberculosis. Another basic objection was the belief that widespread use of BCG vaccine would cancel out permanently the effectiveness of the tuberculin test. BCG causes all persons who have been vaccinated to react to the tuberculin test.

When BCG was first proposed more than 30 years ago, the suggestion was made that its use would be especially desirable in socially impoverished areas with overcrowding and bad housing and perhaps among the Indians who had an exceedingly high death rate. The report of the committee makes no specific reference to such groups.

Mortality rates from tuberculosis in the United States are exceedingly low. They compare quite favorably with those of white populations in other countries, notwithstanding the fact that those populations had been vaccinated with BCG, whereas such vaccination in the United States has been minimal. Furthermore the committee recognizes that BCG is not a positive preventive of tuberculosis, the rates of its effectiveness varying anywhere from 0 to 80 per cent.

In view of all of these facts, the committee did not believe that any further mass experimentation with BCG should be contemplated in the United States. The committee did say, however, that controlled studies on population groups already begun should be continued as long as they furnish significant information.

MORRIS FISHBEIN

ACCIDENTS

ACCIDENTS now are responsible for 7 per cent of the occupancy of beds in American hospitals. In 1956 approximately 95,000 people in the United States died of injuries sustained in accidents. As a cause of death, accidents are outranked only by heart disease, cancer and cerebral hemorrhage. In spite of the intensive campaign that has been carried on for the prevention and control of accidents, the number of motor vehicle accidents continues to rise. A sharp decline has been observed for all other accidents. This signifies that industry particularly has been aware of this hazard and has been making a successful campaign. A recent report from the Health Information Foundation[1] indicates that the death toll of workers from accidents has been reduced from 19,000 in 1928 to 14,300 in 1956. The peak rate was 43 per 100,000 workers in 1937 which declined to 23 per 100,000 workers in 1956. Deaths due to drowning are still substantial in number—4000 in 1956. Railroad safety is outstanding with only 0.20 deaths per 100 million passenger miles. Fatal aviation accidents are still significant, but the largest number occur in private flying. In 1956 the average annual death rate per 100 million passenger miles on scheduled airlines was 0.62 which is slightly greater than the rate for the railroads. A significant number of accidental deaths occurred in the home and about half of these resulted from falls, primarily to people more than 65 years old.

In an attempt to reduce the number of deaths from motor accidents, automobile manufacturers have begun to build protective mechanisms into motorcars. These include safety belts, doors that remain closed under impact, flexible steering wheels, and dashboards that have no protrusions and are covered with shock-absorbing material. Recently in a survey of the problem of motorcar accidents and deaths, the *Lancet*[2] called attention to investigations which have established that the greatest single cause of death in traffic accidents is ejection of the passengers, regardless of the speed at which the car has been traveling. The risk of sustaining injury is twice as great for a person thrown out of a car as for those remaining inside. The use of the safety belt and improved latches and similar door-locking devices can help reduce this hazard.

Next to the possibility of being thrown out of the car as a cause of severe injuries is the impact of the steering wheel and post. The inventors are doing their best to find some method of minimizing this hazard without introducing new difficulties.

Throughout the world extensive studies are being made of hazards which cause accidents and some remarkable facts have been determined relative to the driving of motorcars.

Apparently physical examinations of drivers are not especially helpful, since the mechanism which results in the driver becoming unconscious, blacking out or even dying suddenly is almost always a transient mild derangement of his functions rather than any long-standing infirmity. A factor called "skill fatigue" has been found which is not necessarily accompanied by physical tiredness. Sixty per cent of road transport accidents occur during the first three hours of journeys. After skill fatigue, the second most important cause in lowering driving standards is the drinking of alcohol. Also, in motorcars, while escaping carbon monoxide caused by small leaks in the exhaust system or by gas sucked into the car by ventilation may not be sufficient to produce death, it still may be enough to lower significantly the driver's powers of concentration, interfere with his coordinated thoughts and movements, impair his vision and lead him into emotional and physical lethargy. After an hour, concentrations of more than one-tenth of 1 per cent can be dangerous to life. Some studies made in one laboratory have determined that the danger to the driver is especially great when he is a heavy smoker who already has some accumulation of carbon monoxide in his blood.

During the winter months a rise occurs in the incidence of deaths due to poisoning by illuminating gas and gas from motor exhausts. About 850 deaths were recorded in 1956 as due to poisonous gas in the home. A British investigator has noted that accidental poisoning from gas in the home is most likely to affect people more than 60 years of age. In 1955 of a total of 8000 fatal home accidents in Great Britain, 892 were due to domestic gas and three-fourths of these occurred in people more than 60 years of age.[3] People who grow older not only decline in their ability to see, hear and remember but also in their ability to detect odors. Experiments made to determine the exact facts indicated that 30 per cent of old people cannot reliably recognize the odor of escaping gas at concentrations below 50 per 10,000; whereas, younger people were able to recognize this amount in practically every instance. Consideration is being given to the possibility of adding strong odors to illuminating and heating gas so as to provide a danger signal for accidental escape of unburned gas. In Great Britain there are 1.5 million one person households of which two-thirds are occupied by people more than 60 years old. Obviously, the hazard of escaping gas for these people is a constant one.

The need for intensive research into the causes of accidents is obvious from the high place which accidental deaths have now assumed among the causes of mortality. It seems inevitable that heart disease or heart-failure will remain the leading cause of death, even if the results of research will prevent great numbers of deaths from this condition during youth. Extensive research may diminish greatly the incidence of cancer as well as deaths from this cause. The concentration now apparent on determining the mechanism of atherosclerosis and associated deaths from brain hemorrhage will certainly lower the number of deaths resulting from these conditions. The increasing speed of transportation, the introduction of new hazards in industry, and the increasing age of the population are factors which must constantly tend to increase the number of deaths from accidents. However, practically all accidental deaths should be preventable. Scientific study as to causes, both direct and contributing, will do much to decrease the alarming rise in incidence of accidental deaths.

MORRIS FISHBEIN

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Edema and Hypertension

EDEMA

1. 'DIURIL' is an entirely new, orally effective, nonmercurial agent—1 Gm. of 'DIURIL' orally being approximately equivalent to 1 cc. of mercurial I.M.
2. 'DIURIL' is ideal for initiating diuresis and for prolonged maintenance of the edema-free state.
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any indication for diuresis is an indication for 'DIURIL'

INDICATIONS: Congestive heart failure; premenstrual edema; edema of pregnancy; renal edema—nephrosis, nephritis; cirrhosis with ascites; drug-induced edema. May be of value to relieve fluid retention complicating obesity.

DOSAGE RANGE: one 500 mg. tablet 'DIURIL' to two 500 mg. tablets 'DIURIL' once or twice a day.

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SUPPLIED: 250 mg. and 500 mg. scored tablets of 'DIURIL' (Chlorothiazide); bottles of 100 and 1,000.

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New *for your armamentarium*

Information published in this department is supplied by the manufacturers of the products described.

• "CASTLE 19" OBSTETRIC LIGHT

DESCRIPTION: Featuring two independently adjustable lampheads mounted on separate pantograph arms, this ceiling-suspended light enables the obstetrician to transilluminate his field from widely divergent angles at the table's end. Each lamphead consists of a 17 in. reflector which is guaranteed against clouding, oxidizing or peeling during the life of the unit. The replaceable bulbs are 150 W and have a rated life of not less than 200 hours. Its illumination is filtered against color, heat and glare. and against any appreciable shadows cast by the hands of surgeons or assisting personnel. The intensity of illumination 42 in. from the face of each lamp is specified as not less than 2000 foot-candles, or 4000 foot-candles when focused together. The lampheads are held by horizontal crossarms which provide a total extension of 49 in. from the center of the lamphead to the center of the supporting stem; they also permit 200 degrees rotation and 21 in. vertical adjustment, and enable the lampheads to be tilted at least 180 degrees and to be moved through the horizontal plane at least 210 degrees.
PRODUCER: Wilmot Castle Company, Rochester, N.Y.

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PURPOSE: Treatment of the common cough.
COMPOSITION: Dimethoxanate hydrochloride.
DESCRIPTION: This nonaddictive compound subdues but does not abolish the cough reflex. Its local anesthetic and demulcent action gives almost immediate relief from throat irritations, with subsequent sustained moderation of the cough reflex lasting four to six hours or longer. Antitussive action is equal to ¼ gr. codeine per teaspoon (5 cc.) dose. The mild musculotropic spasmolytic action guards against bronchospasm and possible harmful effects from cough aggravation.
DOSAGE AND ADMINISTRATION: For adults and for children more than eight years old, 1 to 2 teaspoonfuls (25 to 50 mg.) three or four times daily.
HOW SUPPLIED: In 16 fl. oz. and 1 gal. bottles.
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(Continued on page A-102)

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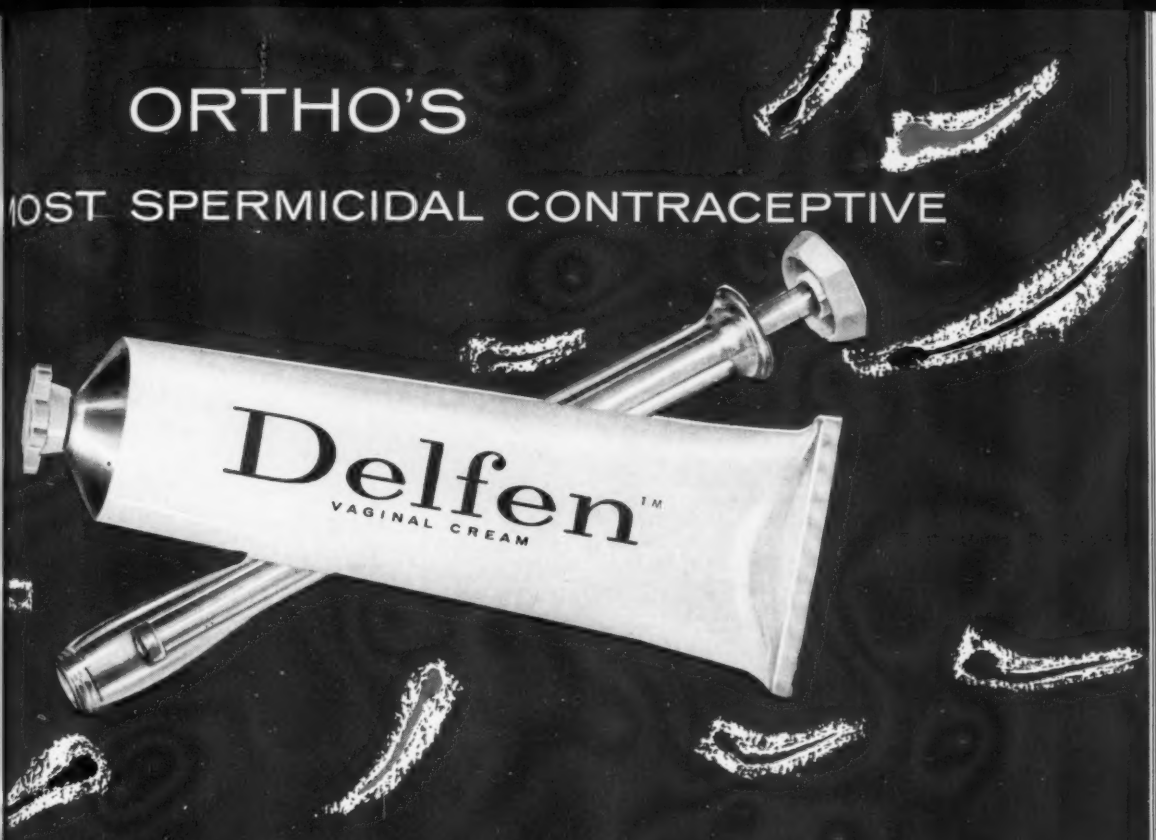

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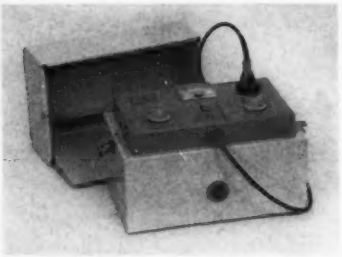
Sobrel, D.; Clark, F.; Jennings, M.; Pelfrey, V.; Olson, N.; Wolf, L.; and Tyler, E. T.: West. J. Surg. 64: 152, 1956.

Composition: nonylphenoxypolyethoxyethanol 5% in an oil-in-water emulsion at pH 4.5.



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PRODUCER: The Birtcher Corporation, Los Angeles.

• PHENERGAN® SUPPOSITORIES (New Dosage Form)

PURPOSE: To provide antihistaminic therapy.
COMPOSITION: Each suppository contains 25 mg. of promethazine hydrochloride.
INDICATIONS FOR USE: Before and after operations, emesis, allergic conditions and swelling, pain and trismus in dentistry.
HOW SUPPLIED: Boxes of 12.
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PURPOSE: To relieve nasal congestion by oral administration.
COMPOSITION: Pseudo-ephedrine hydrochloride in tablet form.
INDICATIONS FOR USE: Acute coryza, vasomotor rhinitis, allergic rhinitis, acute and subacute sinusitis, acute otitis media, acute eustachian salpingitis, serous otitis media with eustachian tube congestion, aero-otitis media and asthma.
DOSAGE AND ADMINISTRATION: Adults and older children, 60 mg. three or four times daily. Infants and children up to six years of age, as directed by a physician.
HOW SUPPLIED: 30 mg. sugar-coated and 60 mg. scored, uncoated tablets in bottles of 100.
PRODUCER: Burroughs Wellcome & Co. (U.S.A.) Inc., Tuckahoe, N.Y.

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PURPOSE: Treatment of physiologic and pathologic effects of nasal allergies.
COMPOSITION: Hydrocortisone, phenylephrine hydrochloride, gramicidin crystalline, neomycin sulfate, methapyrilene hydrochloride and polymyxin B sulfate in a buffered aqueous solution.
INDICATIONS FOR USE: Acute, chronic and perennial rhinitis, nasopharyngitis, seasonal and nonseasonal allergic rhinitis without polyps, and in sinusitis to shrink mucous membranes and improve drainage.
HOW SUPPLIED: 20 cc. plastic spray bottles.
PRODUCER: Philadelphia Ampoule Laboratories, Philadelphia.

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PURPOSE: To facilitate the localization and extraction of renal calculi.
DESCRIPTION: Direct visualization of calculi during surgery is made possible since the screen can be sterilized and placed in the wound immediately adjacent the kidney. Proximity of the screen to the kidney holds image distortion to a minimum. The high-contrast screen is mounted on a lead glass, then sealed in a durable, transparent plastic container measuring 10 by 7.5 by 1.5 cm. The unit after sterilization by immersion in aqueous ZEPHIRAN® for 20 minutes is ready for use. To utilize the unit, an extension cone with a lead diaphragm is adapted to the operating room x-ray unit. This confines radiation to the FG-S screen, thereby minimizing roentgen units during fluoroscopic procedure. The technic enables the visualization of renal calculi as small as 0.25 cm.
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PURPOSE: To alleviate symptoms in bronchial asthma and acute episodes associated with heart-failure.
COMPOSITION: Clysmathane is a 37 ml. solution containing 0.625 gm. of theophylline monoethanolamine (THEAMIN®).
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DOSAGE AND ADMINISTRATION: One unit administered as a retention enema before retiring or as the physician may direct.
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(Continued on page A-104)

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Thiamine Mononitrate (B_1)	3 mg.
Pyridoxine (B_6)	1 mg.
Niacinamide	10 mg.
Riboflavin (B_2)	2 mg.
Vitamin B_{12}	2 mcgm.
Ascorbic Acid (C)	50 mg.
Vitamin K (Menadione)	0.5 mg.
Folic Acid	1 mg.
Ferrous Fumarate	90 mg.
Iron (as Fumarate)	30 mg.
Intrinsic Factor	5 mg.
Fluorine (as CaF_2)	0.015 mg.
Copper (as CuO)	0.15 mg.
Iodine (as KI)	0.01 mg.
Potassium (as K_2SO_4)	0.835 mg.
Manganese (as MnO_2)	0.05 mg.
Magnesium (as MgO)	0.15 mg.
Molybdenum (as $Na_2MoO_4.2H_2O$)	0.025 mg.
Zinc (as ZnO)	0.085 mg.
Calcium Carbonate	575 mg.

Dosage: one or more capsules daily.

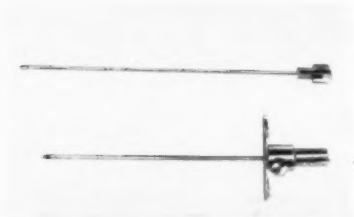
Supplied: attractive, re-usable bottles of 100 capsules.

Lederle LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK

*Trademark

• POCKET pH METER

DESCRIPTION: Weighing only 2 lb., this pocket-sized meter gives a measurement range of 2 to 12 pH with readability of 0.1 pH. Lower values can be measured by a simple adjustment. The instrument has a combination glass and reference electrode, with a 36 in. lead, which may be used while clamped to the instrument's side. Power is supplied by six standard-type batteries. The meter's two tone gray case is made of tough acid-resistant melamine plastic, and has a scratch-resistant polystyrene dial face. A shoulder-type carrying case is also available.
PRODUCER: Scientific Instruments Division, Beckman Instruments, Inc., Fullerton, Calif.



• SIERRA-CHENG EPIDURAL NEEDLE

DESCRIPTION: Intended for use with the anesthetic agent 2-chloroprocaine hydrochloride, the needle is blunt-nosed with an over-all length of 10 cm., of which 8 cm. is graduated in 1 cm. increments so that penetration of the peridural space can be accurately gauged. A flange, secured by a knurled setscrew, provides a means of grasping the needle while penetration of the supraspinous and interspinous ligaments is accomplished, and it can then be moved down the needle until it contacts the skin. A stylet, which is removed before the needle is introduced into the epidural space, lies flush with the contour of the needle to preclude trauma when the needle is inserted.
PRODUCER: R. A. Hawks Division, Sierra Engineering Co., Sierra Madre, Calif.

• NEUTRAPEN

PURPOSE: Management and treatment of allergic reactions to penicillin.
COMPOSITION: Purified injectable penicillinase.
DESCRIPTION: Acting within an hour, the drug reduces the severity and duration of both moderate and severe reactions by neutralizing the circulating penicillin. It relieves itching promptly, clears most reactions in 12 to 96 hours and is nontoxic. The drug remains active in the body fluids for at least four days and may be used prophylactically. Stable at room temperature in the dry state, it must be refrigerated and used within a week when reconstituted with sterile, distilled water.
DOSAGE AND ADMINISTRATION: 800,000 units, usually administered intramuscularly. If reaction recurs or clinical response is delayed, a second injection should be given in three to four days. In anaphylactic reactions 800,000 units should be given intravenously, immediately followed by 800,000 units administered intramuscularly.
HOW SUPPLIED: In single-dose vials containing 800,000 units of injectable penicillinase as lyophilized powder, available singly or in cartons of 12.
PRODUCER: SchenLabs Pharmaceuticals, Inc., New York.

• ELECTRIC AERATOR (Model M-333)

DESCRIPTION: This portable and self-contained aerating unit includes an unbreakable nylon agitator and a 1 qt. polyethylene container designed for maximum turbulence and minimum vortex action. The special knee-action design of the device permits the container to be put in place or removed without tilting. The standard agitator spins at 3000 rpm forcing up to 270 cu. in. of air per minute through the liquid depending on its consistency. Other degrees of aeration may be obtained with various accessory agitators. The unit weighs 8 lb., is 10⅜ in. high, and has a stain-resistant, white refrigerator finish.
PRODUCER: Burgess Vibrocrafters Inc., Grayslake, Ill.

(Continued on page A-106)

help reduce
the pressures
IN your
patients

help reduce
the pressures
ON your
patients

for total management of your hypertensive patients rely upon

RAUDIXIN

Squibb Whole Root Rauwolfia Serpentina

Raudixin provides gradual, sustained lowering of blood pressure in hypertensive patients, as well as a mild bradycardia. Hence, the work load of the heart is reduced.

"... often preferred to reserpine in private practice because of the additional activity of the whole root."

Corrin, K. M.: Am. Pract. & Dig. Treatment 8:721 (May) 1957.

Tranquilizing Raudixin helps relax the anxious hypertensive patient so that he is better able to cope with external pressures without being overwhelmed by them. By reducing these anxieties and tensions, Raudixin helps break the mental tension —hypertension cycle.

Dosage: Two 100 mg. tablets once daily; may be adjusted within range of 50 to 300 mg. *Supply:* 50 and 100 mg. tablets. Bottles of 100, 1000 and 5000.

SQUIBB *Squibb Quality—the Priceless Ingredient*

"RAUDIXIN" IS A SQUIBB TRADEMARK

• MOBILE "200" X-RAY UNIT

DESCRIPTION: Unit has more than double the power of conventional mobile x-ray equipment. It operates at 200 milliamperes, permitting a shorter exposure time and preventing blurring of the image. A rotating-target x-ray tube permits the use of the same small x-ray source as in deluxe machines. It is equipped with an electronic timer. A filament stabilizer insures uniform current to the x-ray tube. An accordionlike extension arm extends the x-ray tube over the bedside for a travel of 20 in. and the tube head rotates 360° above the vertical and through 60° on its own axis within the mounting form. A film carrier in the cabinet of the unit provides storage space for six 14 by 17 in. film holders.
PRODUCER: General Electric Co., X-ray Department, Milwaukee.

• NIATRIC®

PURPOSE: To relieve symptoms of cerebral vascular damage.
COMPOSITION: Each tablet contains:

Pentylenetetrazole	100 mg.
Nicotinic acid	50 mg.
Ascorbic acid	100 mg.
Bioflavonoids	100 mg.

INDICATIONS FOR USE: Depression, confusion and neurasthenia in geriatric patients.
DOSAGE AND ADMINISTRATION: 1 or 2 tablets three times daily.
HOW SUPPLIED: Bottles of 100 and 500.
PRODUCER: B. F. Ascher & Company, Inc., Kansas City, Mo.

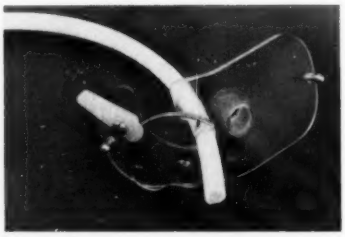
• PEN-VEE® L-A

PURPOSE: Treatment of infections caused by penicillin-sensitive organisms.
COMPOSITION: Each tablet contains 250 mg. (400,000 units) phenoxymethyl penicillin (penicillin V).
DOSAGE AND ADMINISTRATION: Dosage varies with infections treated. Information supplied in manufacturer's literature.
HOW SUPPLIED: Vials of 24.
PRODUCER: Wyeth Laboratories, Philadelphia 1.

• SMITH AUTOMATIC PERFORATOR DRILL

TO START — Press drill down to engage locking mechanism in driving position.
DRILLING — Maintain constant, firm pressure. Drill will automatically disengage upon completion of opening.

DESCRIPTION: The instant the drill breaks through the inner table of the skull, a disengaging mechanism stops the drilling action, thereby protecting the dura against possible injury. Complete with interchangeable drive shanks, the instrument may be used with either a Hudson hand brace or a variable-speed cranial drill. The motor develops a maximum speed of 1100 rpm with an approximate power rating of three-eighths horsepower. The entire unit can be autoclaved.
PRODUCER: Codman and Shurtleff, Inc., Boston.



• BITE BLOCK AND TUBE HOLDER

DESCRIPTION: The transparent acrylic (vinyl) unit incorporates a tubular bite block and a positive locking mechanism to secure the tube which can be inserted after the adapter has been fitted. The tubular shape of the bite block permits suctioning without disturbing the tube, and the clearness of the plastic allows the anesthesiologist to observe the character of the lips and oral cavity at all times. To prevent trauma, the unit is designed with an indentation for the lips and the head strap can be tightened at will without pressing the lips against the teeth.
PRODUCER: R. A. Hawks Division, Sierra Engineering Co., Sierra Madre, Calif.

(Continued on page A-108)

New...from Pfizer Research

84

compounds tested

1

compound unexcelled

Progress has been made in antibiotic therapy through the use of absorption-enhancing agents, resulting in higher, more effective antibiotic blood levels.

For the past two years, in a continuing search for more effective agents for enhancing oral antibiotic blood levels, our Research Laboratories screened eighty-four adjuvants, including sorbitol, citric acid, sodium hexametaphosphate, and other organic acids and chelating agents as well as phosphate complex and other analogs. After months of intensive comparative testing, glucosamine proved to be the absorption-enhancing agent of choice. Here's why:

1 Crossover tests show that average blood levels achieved with glucosamine were markedly higher than those of other enhancing agents screened. In some cases this effect was more than double.

2 Of great importance to the practicing physician is the consistency of the blood level enhancement achieved with glucosamine. Extensive tests show that the enhancing effect with glucosamine occurs in a greater percentage of cases than with any other agent screened.

3 Glucosamine is a nontoxic physiologic metabolite occurring naturally and widely in human secretions, tissues and organs. It is nonirritating to the stomach, does not increase gastric secretion, is sodium free and releases only four calories of energy per gram. Also, there is evidence that glucosamine may favorably influence the bacterial flora of the intestinal tract.

For these reasons glucosamine provides you with an important new adjuvant for better enhancement of antibiotic blood levels. Tetracycline, potentiated physiologically with glucosamine, is now available to you as COSA-TETRACYN.

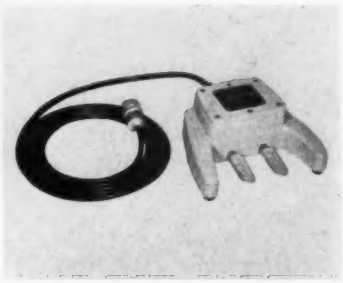
Capsules 250 mg. and 125 mg.

COSA-TETRACYN*

GLUCOSAMINE-POTENTIATED TETRACYCLINE

The most widely used broad-spectrum antibiotic now potentiated with glucosamine, the enhancing agent of choice

*Trademark



• SEALED FOOTSWITCHES

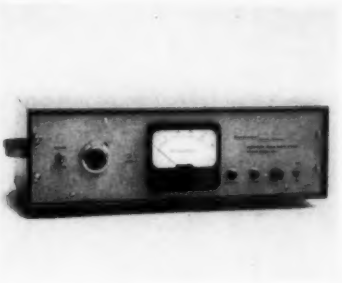
DESCRIPTION: Designed for operation of electric and electronic equipment in the presence of explosive gases, these two explosion-proof switches, single pedal and double pedal (shown here), are each rated at 15 amp. for use with 125 V AC. They have 12 ft. of flexible-type S cords with locking Cannon connectors and receptacles and are finished in light blue crinkle enamel. All electric contact points are contained within sealed cast aluminum housing to conform with U.L. specifications.
PRODUCER: The Birtcher Corporation, Los Angeles.

• DARTAL® TABLETS

PURPOSE: Control of excessive psychomotor and emotional activity.
COMPOSITION: 1-(2-acetoxyethyl)-4-(3-[2-chloro-10-phenothiazinyl] propyl) piperazine dihydrochloride.
DOSAGE AND ADMINISTRATION: For anxiety tension, psychosomatic disorders and other neuroses, 5 mg. three times daily; for psychotic conditions, 10 mg. three times daily. Dosages should be adjusted upward or downward in units of 5 or 10 mg. at intervals of three or four days, according to the needs and response of the patient.
HOW SUPPLIED: 5 and 10 mg. tablets in bottles of 50 and 500.
PRODUCER: G. D. Searle & Co., Chicago.

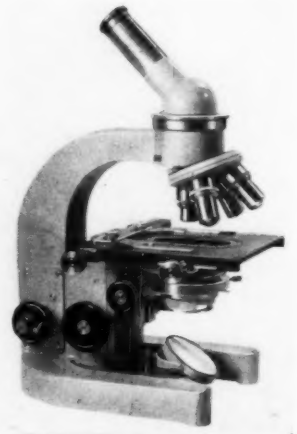
• CHILDREN'S SLIMETTE HEARING GLASSES

DESCRIPTION: Providing true binaural hearing, each temple of these glasses is equipped with a complete hearing-aid circuit. It includes three transistors, an aspirin-sized mercury cell battery, printed circuit, microphone and other components. Each side can be individually fitted to the ear's particular loss and includes volume controls which can be adjusted to the hearing ability of the ear it serves. Available in sizes to fit very young as well as older children, the glasses have pencil-thin temples in either blackwood or redwood plastic matched with fronts of either gold or silver trim and rims.
PRODUCER: Beltone Hearing Aid Co., Chicago.



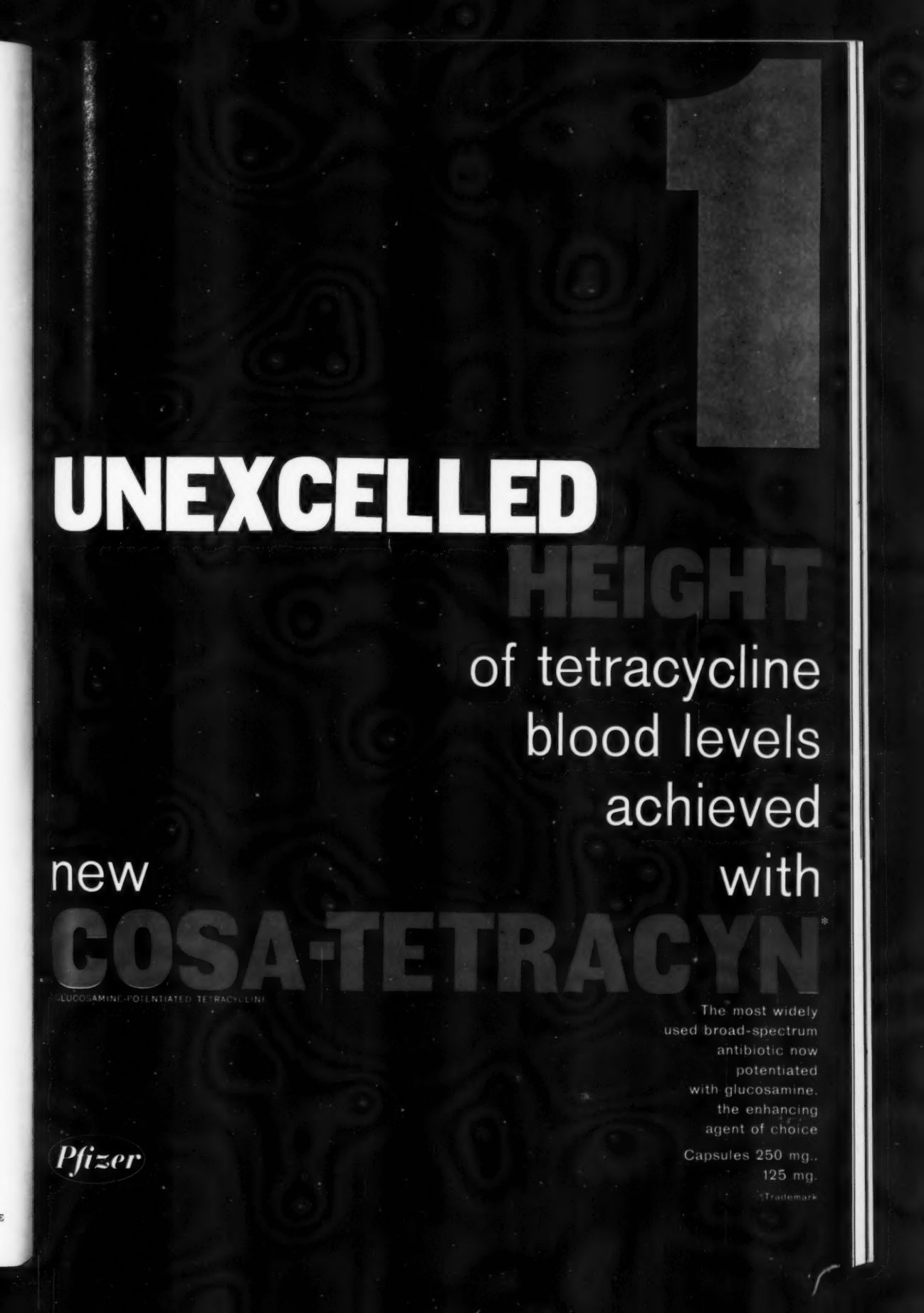
• MEDICAL GAS ANALYZER (Model LB-1)

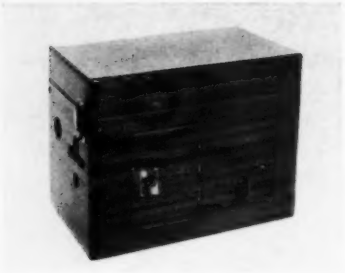
DESCRIPTION: For measuring the concentrations of various gases, this infrared analyzer uses detector cells sensitive to the gas. The cells can be interchanged to allow measurement of carbon dioxide, nitrous oxide, cyclopropane, etc.
PRODUCER: Spinco Division, Beckman Instruments, Inc., Palo Alto, Calif.



• BLEEKER RESEARCH MICROSCOPE R

DESCRIPTION: Almost completely insensitive to temperature variations, this rigid phase-contrast microscope features a permanently horizontal mechanical focusing stage with verniers and inclined eye tube for rapid focus control and comfortable viewing position. Coarse and fine adjustments are made with the hand resting on the table and with absolute freedom from backlash and lost motion. A built-in stop protects microslides. Standard achromatic and apochromatic objectives, ranging from 2x to 90x (oil immersion), are completely dustproof. Eyepieces of either the huygenian or normal variety range from 5x to 28x.
PRODUCER: Karl Heitz, Inc., New York.
(Continued on page A-110)


1
UNEXCELLED
HEIGHT
of tetracycline
blood levels
achieved
with
new
COSA-TETRACYN*
GLUCOSAMINE-POTENTIATED TETRACYCLINE
The most widely
used broad-spectrum
antibiotic now
potentiated
with glucosamine,
the enhancing
agent of choice
Capsules 250 mg.,
125 mg.
*Trademark
Pfizer



• CARDIOGRAPH CABINET

DESCRIPTION: This durable, solid wood cabinet for housing a cardiograph instrument features a top panel which facilitates operation. Recording paper is fed through the front door of the cabinet and the readings emerge through an opening at one end. At the other end is a cable for a cable power cord. In a variety of hand-rubbed woods, including mahogany, oak and walnut, the cabinet is available in a complete range of sizes and designs and can be made to fit any specifications.
PRODUCER: Scientific Wood Cabinet Company, Belleville, N. J.

• ZACTIRIN®

PURPOSE: To relieve pain.
COMPOSITION: Each tablet contains 75 mg. ethoheptazine citrate and 5 gr. acetylsalicylic acid.
INDICATIONS FOR USE: Joint pains and related disorders (arthritis, bursitis, neuralgia, synovitis) and abdominal, postoperative and low back pains.
CAUTION: Total daily dosage should not exceed 8 tablets.
DOSAGE AND ADMINISTRATION: For moderate to moderately severe pain, 2 tablets three or four times daily; for mild pain, 1 tablet three or four times daily.
HOW SUPPLIED: Bottles of 48.
PRODUCER: Wyeth Laboratories, Philadelphia 1.

• DIPSAL

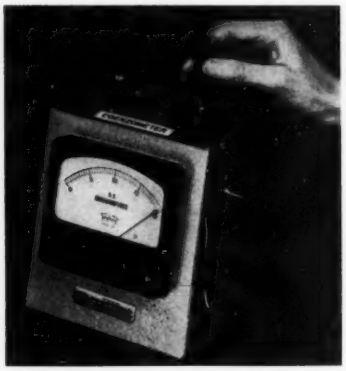
PURPOSE: To relieve pain and muscle spasm.
COMPOSITION: Each tablet contains:

Dipyrone	62.5 mg.
Salicylamide	180.0 mg.
PABA	180.0 mg.
Vitamin C	20.0 mg.
Vitamin B_{12}	2.5 μg.

INDICATIONS FOR USE: Rheumatoid conditions.
DOSAGE AND ADMINISTRATION: 1 or 2 tablets initially, followed by 1 tablet every four hours as required.
HOW SUPPLIED: Bottles of 100 and 1000.
PRODUCER: U. S. Standard Products Company, Mount Prospect, Ill.

• RAPPAPORT-SPRAGUE STETHOSCOPE (Model 280)

DESCRIPTION: Designed for increased efficiency in discerning threshold sounds and murmurs, this instrument will permit accentuation of certain portions of the auscultatory spectrum by means of five chest pieces: adult diaphragm for high-pitched murmurs; 1 in. open bell for localization of low- and medium-pitched sounds; 1⅜ in. open bell for detection of low- and medium-pitched sounds; pediatric diaphragm for high-pitched sounds, and ¾ in. open bell for low- and medium-pitched sounds in infants. Regular, tapered and extra-large types of earpieces are provided; the length of the instrument is 20 in.
PRODUCER: Sanborn Company, Waltham, Mass.



• COENZOMETER

DESCRIPTION: Essentially a single-wavelength, narrow-band spectrophotometer, this instrument precisely measures absorbency and optical density changes in the range of 350 mμ. It is designed for the quick and reliable analysis of transaminase, lactic dehydrogenase, blood alcohol, turbidity and pyridine nucleotides. The spectrophotometer can be used with both commercially prepared reaction mixtures and standard 13 by 100 mm. culture tubes. It operates on standard AC line, requires no voltage regulation, and gives almost maintenance-free operation because of its simplicity of construction.
PRODUCER: Macalaster Bicknell Company, Cambridge, Mass.

when nausea and vomiting bring a plea for help . . .

suggest first aid with . . .

EMETROL®

[PHOSPHORATED CARBOHYDRATE SOLUTION]

a safe, pleasant-tasting, oral antiemetic . . .

effective in 6 out of 7 cases of functional vomiting[1]—often associated with intestinal "flu" or G.I. grippe. Rapidly effective . . . economical . . . and *safe physiologic action* usually eliminates need for potentially hazardous antiemetic drugs. Also established for safe relief of "morning sickness."[2]

Dose: children, 1 or 2 tsp.; adults, 1 or 2 tbsp.; repeat at 15-minute intervals until vomiting ceases. In bottles of 3 and 16 fl.oz. containing balanced amounts of levulose and dextrose with orthophosphoric acid at optimally adjusted pH. DO NOT DILUTE.

1. Bradley, J. E., et al.: J. Pediat. 38:41, 1951. 2. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. 65:311, 1953.

Kinney®

KINNEY & COMPANY, INC. COLUMBUS, INDIANA

THE MEDICAL *Bookman*

► THE CLOSED TREATMENT OF COMMON FRACTURES

By John Charnley, M.B., Orthopaedic Surgeon, Manchester Royal Infirmary, Manchester, England. Ed. 2. 260 pages, illustrated. 1957, The Williams & Wilkins Company, Baltimore. $10.00.

It is the feeling of the author that, although improved technologic methods have permitted better internal fixation of fractures, delayed union after internal fixation frequently is encountered. The theme of this monograph is that denuding bone ends of their periosteal covering in the case of cortical bone or preventing collapse of fragments toward each other in the case of cancellous bone, in each of which internal fixation produces undesirable factors, is accompanied by the serious risk of artificially depressing the osteogenic activity at any given fracture site. Because of this, the author feels that the conservative treatment of fractures offers much merit, and he discusses those fractures which, in his estimation, are best treated by this means.

The mechanics of the conservative management of fractures, the proper use of plaster-of-paris immobilization, and joint restoration after the healing of fractures are well covered. This book deals primarily with fractures about the shaft of the humerus and of both bones of the forearm and selected fractures of the hand, femur and tibia. Excellent line drawings illustrate technics of reduction, and photographs and reproductions of roentgenograms are well chosen. In most instances, the mechanical factors involved in reducing fractures are explained clearly by diagrams which simplify understanding the maneuvers. Although the author stresses conservative management, he realizes the need and place of operative treatment, and is careful to point out instances in which he feels such management is indicated. Particularly is this true of his commentary on fractures of the tibial shaft. He has grouped such fractures, using simple line drawings, into a classification which presents readily his attitude and ideas.

This text should be of value to anyone wh. may be concerned with the treatment of fractures, but it probably will be of greatest service to those who do not treat fractures as specialists, but who see such lesions only occasionally.

E. W. J.

► THE YEAR BOOK OF OBSTETRICS AND GYNECOLOGY 1957-1958 Year Book Series

Edited by J. P. Greenhill, M.D., Professor of Gynecology, Cook County Graduate School of Medicine, Chicago. 597 pages. 1957, The Year Book Publishers, Inc., Chicago. $7.50.

Concise and well done, this is a fine volume of abstracts of the principal obstetric and gynecologic papers published in American and foreign journals between July 1956 and July 1957. The references are adequate for identification of the original sources, and pertinent editorial comments frequently are added. The book should be valuable both for its many references and for the time-saving abstracts it provides.

L. A. A.

(Continued on page A-130)

NOW—EFFECTIVE STEROID HORMONE THERAPY OF RHEUMATIC AFFECTIONS WITH GREATER SAFETY AND ECONOMY

PABALATE'-HC

Robins

Pabalate with Hydrocortisone

Clinical evidence indicates that, in Pabalate-HC, the synergistic antirheumatoid effects of hydrocortisone, salicylate, para-aminobenzoate, and ascorbic acid achieve satisfactory remission of symptoms in *up to 85% of cases studied*

—*with a much higher degree of safety*

—*even when therapy is maintained for long periods*

—*at significant economy for the patient*

Each tablet of Pabalate-HC contains 2.5 mg. of hydrocortisone—50% more potent than cortisone, yet not more toxic.

FORMULA

ablet:

sone (alcohol) ..... 2.5 mg.
salicylate ..... 0.3 Gm.
para-aminobenzoate.. 0.3 Gm.
id .....50.0 mg.

Two tablets four times daily.
l information on request.

AVAILABLE FOR YOUR PRESCRIPTION NOW

A. H. ROBINS CO., INC. RICHMOND 20, VIRGINIA
Ethical Pharmaceuticals of Merit since 1878

► LABORATORY APPLICATIONS IN CLINICAL PEDIATRICS

By Irving J. Wolman, M.D., Director of Laboratories and Hematologist, The Children's Hospital, Philadelphia. 1,019 pages. 1957, The Blakiston Division, McGraw-Hill Book Company, Inc., New York, Toronto and London. $15.00.

Although this book of 80 chapters will probably interest pediatricians and general practitioners, it is almost too pretentious. The author has succeeded in including nearly everything that his broad experience has taught him. The bibliographies at the end of each chapter doubtlessly authenticate statements made; however, no author's name is definitely mentioned in the text.

Twenty-seven chapters are devoted to hematology, including one chapter on the spleen and three on bone marrow. Other subjects covered are urinalysis and kidney diseases, cerebrospinal fluid, diseases of the liver, blood chemistry, the gastrointestinal tract, the endocrine system, infectious diseases, chemotherapy, obscure diseases, and poisonings.

There are no illustrations. Nor are any technics given. The author has had vast experience as a pathologist and a clinical pathologist, and one wishes that he would have indicated his preference for methods, and had used photomicrographs and drawings rather than so many words.

As a book of reference to considerable of the literature in pediatrics and to differences in findings in children as compared with those in adults, this volume will be useful.

A. H. S.

► OCCUPATIONAL DISEASES OF THE SKIN

By Louis Schwartz, M.D., retired Medical Director, United States Public Health Service, Louis Tulipan, M.D., Emeritus Clinical Professor of Dermatology, New York University-Bellevue Post-Graduate Medical School, New York City, and Donald J. Birmingham, M.D., Medical Director, United States Public Health Service, Washington, D.C. Ed. 3. 981 pages with 189 illustrations and two plates in color. 1957, Lea & Febiger, Philadelphia. $18.00.

Some very interesting new work has been included in this edition that will particularly assist the employee, safety engineer, plant physician and insurance carrier to a better understanding of industrial skin hazards, and thus lower the incidence of industrial dermatitis.

Especially informative are the chapters on skin hazards from atomic radiation, chromate dermatitis, and the process of cross-sensitization with other metals such as zinc. The additional information on dermatoses caused by synthetic resins and resin glues is most interesting. Some new color plates are included which aid in bringing out the appearance of various occupational diseases of the skin.

This book is highly recommended to all those who are interested in diseases of industry.

J. H. L.

► METHODS IN SURGICAL PATHOLOGY

By Henry A. Teloh, M.D., Assistant Professor of Pathology, Northwestern University Medical School, Chicago. 127 pages. 1957, Charles C Thomas, Springfield, Illinois. $4.75.

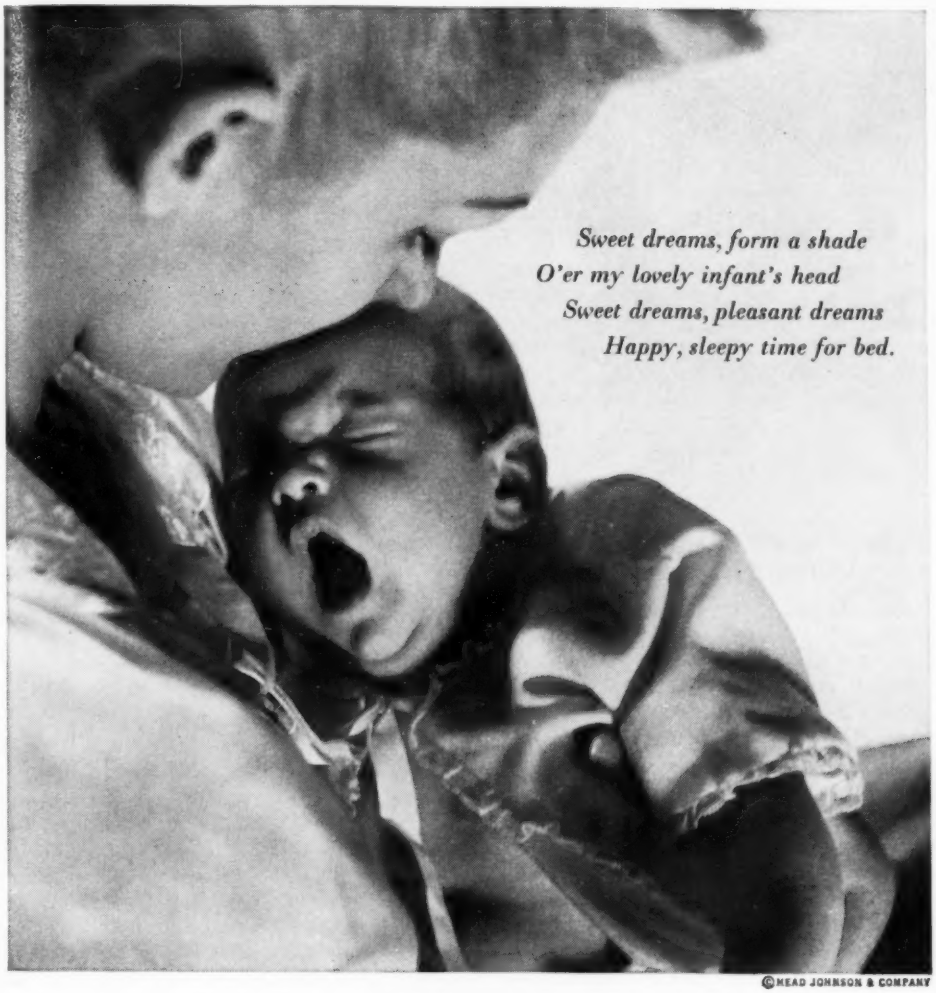
Intended as a guide book for the resident working in the surgical pathology laboratory, this small volume contains 36 brief chapters. It also has an appendix in which four illustrative cases are presented with descriptions of gross and microscopic examination and diagnosis. The "embryo" pathologist who is familiar only with the technics of postmortem examinations will find here definite advice on laboratory procedures in which prompt action, teamwork and knowledge are most important.

Throughout the book, certain responsibilities of the pathologist are emphasized. While he is not responsible for material until it is in his hands, the pathologist should receive the material as soon as possible after it has been removed. Its care, including weighing, prevention of drying, expert examination, selection of the block, method of cutting, straining, mounting, microscopic examination, consultation with the surgeon, keeping of the records, and many other details become his responsibility. Procedures of handling material from the most frequently performed operations are discussed.

The figures in the book are all from line drawings; while they are very clear, it would seem that the reader might learn more from illustrations made from good photographs.

A. H. S.

(Continued on page A-132)



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You can specify PABLUM BRAND ® *with confidence*

Pablum High Protein Cereal was created to help meet baby's protein needs during the first year of growth. It is 35% protein, a level much higher than in many foods known for high protein content. It satisfies baby's hunger for longer periods of time—longer *night* periods. Babies also relish Pablum Mixed Cereal, Rice Cereal, Barley Cereal and Oatmeal . . .

the baby cereals made to pharmaceutical standards of quality—especially processed for extra smoothness and lasting freshness.

Pablum Products DIVISION OF MEAD JOHNSON & CO., EVANSVILLE, INDIANA • MANUFACTURERS OF NUTRITIONAL AND PHARMACEUTICAL PRODUCTS.

► OCCIPITOPOSTERIOR POSITIONS

By Edward L. King, M.D., Professor Emeritus of Obstetrics, Tulane University School of Medicine, New Orleans. American Lecture Series. 106 pages, illustrated. 1957, Charles C Thomas, Springfield, Illinois. $3.75.

Presenting a good practical review of the subject of occipitoposterior positions, this monograph begins with a discussion of the general aspects, etiologic factors and conduct of labor. It includes a careful description of both nonoperative and operative procedures for delivery. Special reference is made to the Scanzoni method, the DeLee key-in-lock procedure, and the use of the Kjelland and Barton forceps. This well-illustrated text should be of value to students of obstetrics as well as to practicing obstetricians.

L. A. A.

► DIAGNOSIS AND TREATMENT OF CARDIOVASCULAR DISEASE

Edited by William D. Stroud, M.D., Professor of Cardiology, University of Pennsylvania Graduate School of Medicine, Philadelphia, and Morris W. Stroud, III, M.D., Associate Professor of Medicine, Western Reserve University, Cleveland. Vol. 1 and 2. 1,702 pages, illustrated. 1957, F. A. Davis Company, Philadelphia. $35.00.

Rapid progress in the field of cardiovascular diseases during a single generation has necessitated frequent editions of this book. Containing contributions from 59 of the more prominent American leaders in this branch of medicine and surgery and covering every aspect of diagnosis, prognosis and treatment of heart disease, the text is in two volumes of loose-leaf structure so that minor revisions may easily be kept up to date.

The material covers basic phases such as features of the normal heart, heart sounds, normal blood pressure and its variations, disturbances of the heart beat, ballistocardiography, and electrocardiography. The section of electrocardiography consists of 158 pages and, in the estimation of the authors, shows practically every form of abnormal electrocardiographic tracing.

Each major section in the book is written as a separate unit, containing a historical background, basic principles and clinical application, and is accompanied by a fairly complete bibliography. Some of the subjects discussed are: congenital abnormalities, rheumatic fever, cardiac hypertrophy, hypertension, congestive heart-failure, the heart in pregnancy, and heart disease and various endocrine gland disorders. The illustrations include schematic drawings, reproductions of x-rays, and photographs.

Unlike other current textbooks, which are somewhat deficient in this regard, this text includes the very latest methods in intracardiac surgery. The last portion of volume 2 covers roentgenology of the heart and great vessels and peripheral vascular disease, both arterial and venous. The various sections on therapy describe the indications for and give the actions of drugs, dosages and evaluation of therapy.

Y. S.

► A SYNOPSIS OF CHILDREN'S DISEASES

By John Rendle-Short, D.C.H., Lecturer in Child Health, University of Sheffield, Sheffield, England. 624 pages. Ed. 2. 1957, John Wright & Sons Ltd., Bristol, England. Distributed by The Williams & Wilkins Company, Baltimore. $7.00.

First appearing in 1953, this handy reference volume has found a place in pediatric literature. Printed in synopsis form, it furnishes a wide range of information regarding both usual and unusual conditions in infants and children for one who would like to know the essential details at short notice, leaving more detailed study for another time and place. The volume should be helpful to the busy practitioner as well as to the student preparing for pediatric examinations.

This book is open to the criticism that it deals dogmatically with controversial subjects. However, it is not its purpose to present all aspects of diagnosis and treatment. When there are major differences of opinion, the prevailing concept is given.

Although the author has drawn his information from British sources, he has also consulted the well-known American text, Nelson's "Textbook of Pediatrics," to familiarize himself with pediatric thinking on this side of the Atlantic.

The book is compact, well organized and printed and up to date on current therapeutic procedures and the newer disorders of pediatric interest. A few useful tables and illustrations enhance its value.

S. D. M.

(Continued on page A-135)

► EAR, NOSE AND THROAT DYSFUNCTIONS DUE TO DEFICIENCIES AND IMBALANCES

By Sam E. Roberts, M.D., Associate Professor of Otolaryngology, University of Kansas School of Medicine, Kansas City, Kansas. 323 pages, illustrated. 1957, Charles C Thomas, Springfield, Illinois. $8.50.

A completely different and extremely sensible approach to dysfunction of the ear, nose and throat, based on many years of practice and clinical observation, is presented. Rather than the usual circumscribed segmental approach, Dr. Roberts has used the total approach to the control of headaches, allergies, tinnitus, Meniere's disease, exhaustion, dysfunctions of the sinuses and acoustic nerve, and many other conditions. The case histories presented help to show the results accomplished by this method of treatment. The philosophical and general discussion of deficiencies and imbalances given in chapter 2 and the chapters on antimetabolites, gonadal imbalances, insulin-sugar imbalance and basic therapy are of particular interest. The author's emphasis on the importance of cellular nutrition and metabolism in disease and dysfunction rather than on the virulence and toxicity of the microorganisms affecting the nose and throat should stimulate others to seek answers to some of the problems presented.

Nose and throat specialists, internists and general practitioners will benefit greatly from this work. In many instances, radical surgery might very well be eliminated if Dr. Roberts' "over-all" concept were adopted.

I. P. F.

► THE DIAGNOSIS AND TREATMENT OF PULMONARY TUBERCULOSIS

By Paul Dufault, M.D., Medical Director of the Rutland State Sanatorium, Massachusetts Department of Public Health, Worcester, Massachusetts. Ed. 2. 426 pages, illustrated. 1957, Lea & Febiger, Philadelphia. $9.00.

The historical aspects of tuberculosis, which are covered briefly, present a working background of the various therapeutic innovations that we have today. The section on the fundamental aspects of tuberculosis, namely, the chemistry of the tubercle bacillus, the laboratory procedures and the pathologic aspects, includes as much detail as a practitioner would need.

Nothing particularly new is presented in the section on differential diagnosis, but the sections on antibiotic and chemotherapeutic agents are up to date and are of extreme practical value. Of particular interest is the author's rather frank discussion of the limitations of physical examination methods, especially the many eponymic maneuvers taught in medical school. The brief review of the various surgical methods employed in tuberculosis includes no statistical results and gives only general statements indicating the use of different procedures.

Briefly discussed in the concluding chapters are tuberculosis in industry, among hospital personnel and in marriage and pregnancy; the social and emotional aspects of the problem of tuberculosis, and the prevention of the disease.

Y. S.

► THE CENTURY OF THE SURGEON

By Jürgen Thorwald. 432 pages with 66 illustrations. 1957, Pantheon Books Inc., New York. $5.95.

Many histories of surgery are available, not only of surgery as a whole but even of special epochs in surgery. In this book the author has adopted a unique device for telling his story. The book is written as though a young man could have seen personally the events recorded here.

Modern surgery begins with the discovery of anesthesia, which is beautifully reported in this book, although without any mention of Oliver Wendell Holmes, who coined the word "anesthesia." The history of surgery is then traced throughout the world, involving such dramatic discoveries as cutting for stone, detecting cancer, plastic surgery, cesarean section, asepsis and many other surgical triumphs. The story of appendicitis is particularly interesting. The accents in this work are often on unusual incidents rather than on the main trend of surgical discovery. Occasionally, the device of the writing gets in the way of the facts and detracts from them.

Both the physician and the surgeon will enjoy this book. It will, moreover, be useful and entertaining to the so-called average reader.

M. F.

(Continued on page A-136)

► DEGENERATIVE CHANGES IN THE STERNOCLAVICULAR AND ACROMIOCLAVICULAR JOINTS IN VARIOUS DECADES

By Anthony F. DePalma, M.D., James Edward Professor and Head of the Department of Orthopedic Surgery, Jefferson Medical College, Philadelphia. American Lecture Series. 178 pages, illustrated. 1957, Charles C Thomas, Springfield, Illinois. $5.50.

A natural sequel to the author's published study of the glenohumeral joint, this monograph on the anatomy of the sternoclavicular and acromioclavicular joints primarily concerns the relationship of symptoms to age and degenerative changes and anatomic variations.

From individuals in an age range of from premature infancy to 95 years, 223 sets of matching sternoclavicular and acromioclavicular joints were obtained post mortem. Conditions found in these joints are tabulated according to decades, with a discussion of the anatomic variations and changes occurring in each decade. In addition to an analysis of the gross changes, an excellent study is presented of the microscopic changes that come with age; both types of change are well illustrated photographically.

Emphasis is placed on the role of the intra-articular disks seen in the acromioclavicular and sternoclavicular joints, the variations seen in these disk structures, and on their function in preventing early development of regressive changes. The first degenerative changes noted in the acromioclavicular joints appear in specimens from the second decade; the first among the sternoclavicular joints are seen in the third decade. Through subsequent age groups, the rise in the increment of change in the articular surface of the joints is rapid.

Because the disks of the sternoclavicular joints can resist severe degenerative changes for several decades, they act not only as buffers but also as effective means of lubrication of the joints throughout the period of use. The roentgenologic changes occur more frequently and more extensively in the acromioclavicular than in the sternoclavicular joints. In general, the roentgenographic changes parallel the gross findings, but they have no correlation with the presence or absence of clinical manifestations in either joint.

The illustrations are adequate and clear-cut. Although information is given on a portion of the physiology and anatomy of the shoulder which previously has not been well known, it is difficult to appreciate the actual clinical application of many of the points emphasized.

E. W. J.

► TEXTBOOK OF PATHOLOGY With Clinical Applications

By Stanley L. Robbins, M.D., Associate Professor of Pathology, Boston University School of Medicine, Boston. 1,351 pages with 993 figures. 1957, W. B. Saunders Company, Philadelphia and London. $18.00.

Although each of several recent texts on pathology is unique in its approach, Dr. Robbins presents the subject in still a somewhat different manner. His objective is to correlate the essential pathologic findings with clinical manifestations of disease processes. Unlike some books on this subject with many contributors, Dr. Robbins has assumed the major responsibility for this text. He has enlisted five authorities to write on different aspects of pathologic alterations: Dr. J. Foley on the nervous system, Dr. I. Glickman on the oral cavity, Dr. F. Parker, Jr. on the lymph nodes and spleen, Dr. G. K. Mallory on the liver, and Dr. H. Mescon on the skin.

There are 32 chapters and an index, and at the end of each chapter are references with a comment by the author concerning each of the articles mentioned. The gross photographs as a whole are good, but the microscopic reproductions in many instances are not clear. Each chapter is preceded by an outline of discussion and covers a review of the embryologic, physiologic and anatomic features of the diseases, the essential pathologic alterations, and the clinical correlation based on the assumption that signs and symptoms of disease follow these alterations.

The terminology is generally that accepted in most areas; however, "red blood cells" and "white blood cells" are used instead of the modern nomenclature, "erythrocytes" and "leukocytes." This newer nomenclature appears in chapter 18 on lymph nodes and the spleen, which is, incidentally, a very good discussion of the subject. The discussion of tuberculosis emphasizes the history and clinical examination but is not as thorough in covering the gross and microscopic changes in granulomatous diseases.

S. A. L.

(Continued on page A-138)

sleep for the sleepless*

*The stroboscopic photo shows movements of restless sleeper (28-year-old male) after placebo. The following night the same patient was given nonbarbiturate Doriden 0.5 Gm. at bedtime. The result was an approximate 50 per cent reduction in overt motion and restlessness. Doriden® (glutethimide CIBA) acts within 15 to 30 minutes; induces 4 to 8 hours of sound, natural sleep; rarely causes morning hangover. **C I B A** Summit, N. J.

► TREVES' STUDENT HANDBOOK OF SURGICAL OPERATIONS

Revised by Sir Cecil Wakely, F.R.C.S., Director of Surgical Studies and Teacher of Operative Surgery, King's College Hospital Medical School, London. Ed. 10. 594 pages, illustrated. 1957, Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York. $7.50.

The purpose for which this book was intended is somewhat difficult to comprehend, for there appears to be no explanation as to why certain operations are discussed and others are omitted. In general, the book appears to be best suited for the advanced student or the general practitioner who does a limited amount of surgery.

More space is given to a discussion on ligature of arteries than seems necessary. Then come the specialty fields, such as operations on nerves, bones and joints and plastic surgery. The latter deals only with cleft lips and palates; no mention is made of other more basic plastic surgery.

The discussion on operations on the face, throat and neck is brief, and the section on surgery of the abdomen is only partially complete. Other chapters cover such subspecialties as neurosurgery, urology, radiotherapy, and, briefly, highly specialized operations.

Y. S.

► THE ELECTROCARDIOGRAM Its Interpretation and Clinical Application

By Louis H. Sigler, M.D., Attending Cardiologist and Chief of Cardiac Clinics, Coney Island Hospital, Brooklyn. Ed. 2. 312 pages, illustrated. 1957, Grune & Stratton, Inc., New York and London. $8.75.

While certain parts of this edition, particularly those dealing with the electric axis, ventricular gradients and cardiac arrhythmias, are well written and treat their subjects satisfactorily, it has many deficiencies for a new book purported to cover the field of electrocardiography. The section on congenital heart disease is brief and inadequate, which is regrettable in view of the current prominence of this phase of cardiology due to the advances in surgical treatment. Also, there is no mention of the concepts founded by the Mexical school of cardiology; and, while these concepts are controversial, they are at the same time most interesting and seem to warrant discussion in a new book on electrocardiography. The discussion of Dr. Prinzmetal's concepts regarding auricular flutter, fibrillation and supraventricular tachycardia comprises one sentence.

The most attractive feature of the book is the excellence of the electrocardiograms used to document myocardial injury and cardiac arrhythmias. Primarily for their sake the work will have some value as a reference source, but the deficiencies mentioned subtract from its usefulness for such a purpose and render it inadequate as a text to cover all of electrocardiography.

R. O. B.

► FUNDAMENTALS OF CLINICAL NEUROPHYSIOLOGY

By Paul O. Chatfield, M.D., formerly Chief, Section of Clinical Neurophysiology, National Institute of Neurological Diseases and Blindness, Bethesda. 392 pages with 150 illustrations. 1957, Charles C Thomas, Springfield, Illinois. $8.50.

From the material gathered in teaching medical students physiology over a period of years, the author has selected what was appropriate for presentation in book form, organized it, and in certain spheres augmented it. The result is very satisfactory from the reader's standpoint. The author states in his preface that he purposely has omitted controversial material. This includes certain phases of neurophysiology, most of which remain as poorly understood phenomena.

In the main, the book is interestingly written and understandable, an achievement which is often difficult in writing on fundamentals of neurophysiology. The numerous illustrations are clear, and they carry adequately explanatory legends. A satisfactory bibliography follows each chapter, and the book is well indexed.

This work does not have the fault of many expositions of neurophysiology in which the author loses himself in detail concerning minute problems of specific nerve actions and interactions, thus confusing the novice who is interested in obtaining a conception of neurophysiology as a whole. As a good basic introduction to the physiology of the nervous system, the book will be a worthwhile addition to the library of students interested in this field.

H. W. D.

(Continued on page A-140)

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► THE CARICATURE OF LOVE
A Discussion of Social, Psychiatric and Literary Manifestations of Pathologic Sexuality

By Hervey Cleckley, M.D., Clinical Professor of Psychiatry and Neurology, Medical College of Georgia, Augusta. 319 pages. 1957, The Ronald Press Company, New York. $6.50.

The author has examined concepts of sexuality held today by psychiatrists and many distinguished writers of essays and fiction. In addition, he has not hesitated to state his own opinions strongly and to support them with evidence from his own patients. Thus he states that Fererczi's concept of sex is without evidence. Especially concerned with current concepts of homosexuality, the author believes that science cannot yet answer whether or not homosexuality is an illness, a vice or a normal state of health. Incidentally, a distinguished British scientific board has apparently just indicated that homosexuality after age 21 is not to be considered abnormal or a crime under British law.

One of the most valuable aspects of this book is the questioning by its author not only of many current views held by leaders in the field of psychoanalysis but also of many of the original freudian writings. But one wonders just how much is to be gained by analyzing the writings of Philip Wylie and other popular writers in the field of sex and even the popular magazines. The quality of the book is somewhat marred by this consideration, although the margin that separates the popular writers of today from such authors as Maupassant, Balzac and Flaubert, who were equally concerned with sexual aberrations, is not too distinct. Especially interesting is the chapter devoted to André Gide, who won the Nobel prize and whose peculiar attitudes on sex have quite clearly been reflections of his own life. The author's study of D. H. Lawrence and the manner in which his attitude toward sex is so fully reflected in his books is one of the most enlightening discussions offered so far in this field. Certainly Dr. Cleckley, through the public's acceptance of his "Three Faces of Eve," has assumed a position of great importance among writers in the field of psychology and psychiatry. This present book shows that his extensive reading and learning warrant his recognition as an author worthy of more than usual notice.

M. F.

► SYSTEMIC ARTERIAL EMBOLISM
Pathogenesis and Prophylaxis

By John Martin Askey, M.D., Associate Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles. 157 pages, illustrated. 1957, Grune & Stratton, Inc., New York and London. $5.75.

In considering the important problem of thrombo-embolism in cardiac disease, the author has gathered and objectively analyzed a great deal of material. He has offered, in concise form, a workable hypothesis for the management of patients with this condition.

The initial chapters are concerned with an analysis of risk, morbidity and mortality and with the clinical correlations of systemic arterial embolism. In three chapters, the author has discussed the pathogenesis of cardiac mural thrombosis and embolization; particularly interesting is the discussion concerning the mobilization of thrombi. In discussing the diagnosis and management of thrombo-embolism, the author's stress on prophylaxis is commendable.

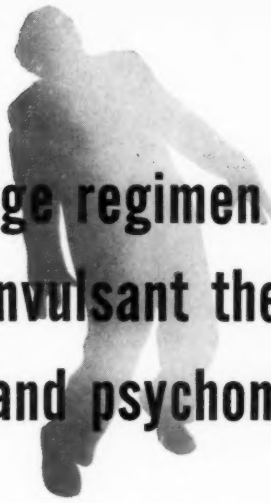
Several controversial issues are presented in the chapter on anticoagulants. It is implied that discontinuing anticoagulant therapy increases the risk of thrombo-embolism over the preanticoagulant risk; however, to date, I am not aware of definite evidence that stopping the use of anticoagulants does any more than restore the risk. The author is satisfied with a 50 per cent reduction of plasma prothrombin activity as a prophylactic measure in thrombo-embolism. Other workers in the field advocate greater reduction of prothrombin activity. Although the author implies that the coagulability of the blood becomes greater with increasing age, I know of no definite proof of this theory.

The discussion with regard to the use of quinidine in auricular fibrillation is limited; in fact, "quinidine" does not appear in the index.

The presentation of statistical material in the form of tables and instructive diagrams is easy to follow. The photographs and drawings are well reproduced. One of the outstanding features of the organization of this text is the clear and concise summary at the end of each chapter. An extensive bibliography is available for those who wish to obtain greater detail on certain points of interest.

J. A. S.

(Continued on page A-144)



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► TECHNIQUE OF FLUID BALANCE
Principles and Management of Water and Electrolyte Therapy

By Geoffrey H. Tovey, M.D., Director, South West Regional Blood Transfusion Service, Southmead, Bristol, England. 100 pages. 1957, Charles C Thomas, Springfield, Illinois. $2.50.

Packed full of information, this small book is presented in clear, understandable language. As may be said of many books by English authors, it is a pleasure to read it just for its precise choice of words. For the general practitioner and the clinical pathologist it will be a guidebook at times in managing the patient in the maintenance of fluid balance.

The preface stresses the need for a short account of the subject, and also that while blood electrolyte estimations made in well-equipped laboratories are of great importance, it must be appreciated that a vast number of patients have to be treated where such analyses cannot be obtained. The author's aim is to guide the doctor who has no laboratory facilities, even though his early training and experience have made him familiar with the need for such determinations.

The nine short chapters contain the volume, distribution and chemical composition of the body fluids; physiology of fluid balance; consequences of depletion of principal body fluid components; maintenance of fluid balance; diagnosis of body fluid deficit; adverse effects of treatment; some special problems of fluid balance, and technic.

The text also includes references to the literature and three appendixes which present basic information.

A. H. S.

Books received are acknowledged in this department. As space permits, books of principal interest to our readers will be reviewed more extensively. Additional listings will be found on pages 155 and 173 of this issue.

The Principles of Therapeutics. By J. Harold Burn, M.D., Professor of Pharmacology, University of Oxford, Oxford. 278 pages, illustrated. 1957, Charles C Thomas, Springfield, Illinois. $5.50.

The Lower Urinary Tract in Childhood; Some Correlated Clinical and Roentgenologic Observations. By Sven Roland Kjellberg, Nils Olof Ericsson and Ulf Rudhe, Stockholm, Sweden. 298 pages with 265 illustrations. 1957, The Year Book Publishers, Inc., Chicago. $18.00.

The Epileptic Seizure; Its Functional Morphology and Diagnostic Significance. By Cosimo Ajmone-Marsan, M.D. and Bruce L. Ralston, M.D., Department of Health, Education and Welfare and the Public Health Service, Bethesda. 251 pages with 47 illustrations. 1957, Charles C Thomas, Springfield, Illinois. $6.00.

Hospital City. The story of the men and women of Bellevue. By John Starr. 282 pages. 1957, Crown Publishers, Inc., New York. $5.00.

There is a Doctor in the House. A Handy Aid Book. Edited by Henry R. Kreider, Ph.D., Director of Research, Chesebrough-Pond's, Inc., New York. 1957, Richards Rosen Associates, Inc., New York.

Diseases of the External Ear. American Lecture Series. By Ben H. Senturia, M.D., Associate Professor of Clinical Otolaryngology, Washington University School of Medicine, St. Louis. 211 pages, illustrated. 1957, Charles C Thomas, Springfield, Illinois. $8.50.

Management of Complications in Eye Surgery; Avoidance of Pitfalls and Treatment of Difficult Situations in Ophthalmologic Operations. Edited by R. M. Fasanella, M.D., Chairman of the Section of Ophthalmology, Yale University School of Medicine, New Haven, with 20 contributors. 422 pages, illustrated. 1957, W. B. Saunders Company, Philadelphia and London. $16.00.

Manual of Pediatric Physical Diagnosis. By Lewis A. Barness, M.D., Associate Professor of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia. 195 pages, illustrated. 1957, The Year Book Publishers, Inc., Chicago. $4.00.

The Bases of Treatment. By Neuton S. Stern, M.D., Associate Professor of Medicine, and Thomas N. Stern, M.D., Instructor in Medicine, University of Tennessee College of Medicine, Memphis. 176 pages. 1957, Charles C Thomas, Springfield, Illinois. $4.75.

Psychiatry and Catholicism. By James H. VanderVeldt, O.F.M., Ph.D., Professor of Psychology, and Robert P. Odenwald, M.D., former Director of the Child Center and Assistant Professor of Psychiatry, The Catholic University of America, Washington, D.C. Ed. 2. 474 pages. 1957, The Blakiston Division, McGraw-Hill Book Company, Inc., New York, Toronto and London. $6.25.

Hormones in Blood; Ciba Foundation Colloquia on Endocrinology. Edited by G. E. W. Wolstenholme, O.B.E. and Elaine C. P. Millar, A.H-W.C. Vol. 11. 416 pages with 74 illustrations. 1957, Little, Brown & Company, Boston. $9.00.

The Physician's Own Library. Its Development, Care and Use. By Mary Louise Marshall, Librarian, Rudolph Matas Medical Library, Tulane University of Louisiana, New Orleans. 87 pages. 1957, Charles C Thomas, Springfield, Illinois. $3.00.

The Incurable Wound; Further Narratives of Medical Detection. By Berton Roueché. 177 pages. 1957, Little, Brown & Company, Boston. $3.50.

The Illustrated Birth Control Manual. By Valeria Hopkins Parker, M.D., Charter Member, American Association of Marriage Counsellors, New York. 392 pages with 178 illustrations, including 27 color plates. 1957, Cadillac Publishing Company, Inc., New York. $5.00.

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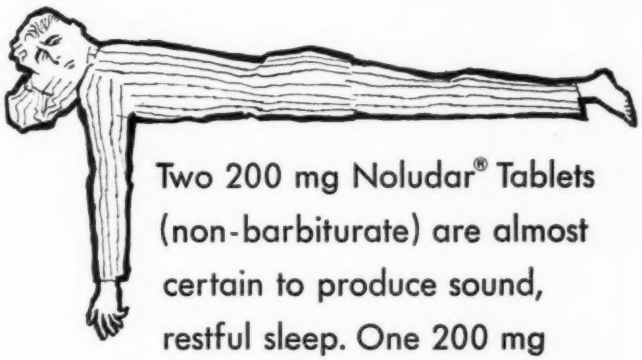

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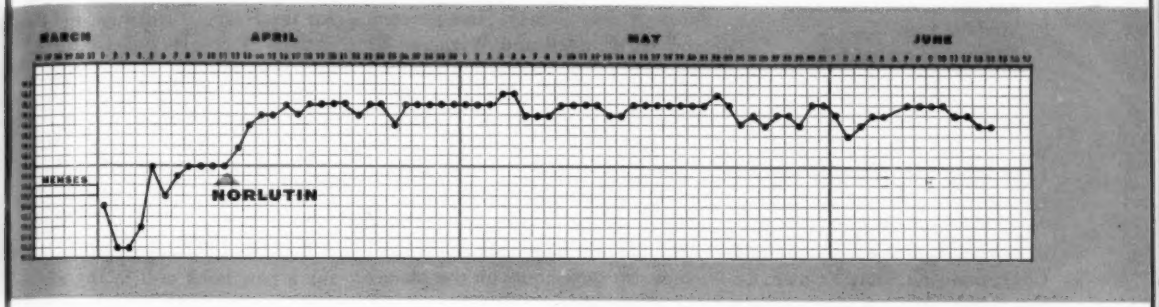

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*Greenblatt, R. B.: *J. Clin. Endocrinol.* **16**:869, 1956.

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DR. Pepys' Pages

Personal Diary
and Observations on
Medical Life
by MORRIS FISHBEIN, M.D.

Dec. 1—This afternoon witnessed a marvelous travelogue of Leonard Bernstein in Israel and his work with the orchestra. Next, to Lester Dragstedt's where came many of the faculty—Coggeshall, Kirsner, Palmer, LeRoy, Aldrich, and many of the young men. For dinner to the Standard Club with the Vatzes and there were the David Mayers and Leonard Bezarks to partake of wild geese shot by Ted Vatz in Canada. And David Mayer told us much about the new coliseum since he is chairman of the board, and he promises that the building will be ready in 1959—which means 1960 for sure.

Dec. 2—To the University, visiting with LeRoy the new automation in medicine—blood cells counted by electronics; oxygen consumption and sugar metabolism continuously measured, and similar procedures.

Dec. 3—For dinner with Mistress Pepys to the annual meeting of the Institute of Medicine where Eric Oldberg read of the distinction of the citizen fellows. Here came Frank Brawley, Archibald Hoyne, and many more of the older medical statesmen. New fellows are the great educator Benjamin Willis of the public schools and Long, who is a brother of Esmond and whose father was the great John of Northwestern. Met here also Johnson of Rockford who was of the Mayos, a disciple of Gordon New. So rode home with the Dragstedts and Maurice Goldblatt.

Dec. 4—By the early plane to Cleveland to speak to the annual meeting of the Cleveland Area Heart Society. Here greeted by Hy Friedell and Wiggers. At the table were Irving Hexter, Newton Baker III and Hartnell of Jones and Laughlin. So spoke of the epidemiology of coronary disease, of statistics, of federated fund raising and of automation in medicine. Thereafter to prepare three radio interviews on tape. So then home on the plane, reading a great detective story by Benson, which is called "The Running Man."

Dec. 5—At noon to the Bismarck for luncheon with Steve Herlitz and his associates to talk of various periodicals. Then to Albert Pick's office to talk with him and Alrod of new work for La Rabida. Next to the Crerar Library and read the *Boston Medical Quarterly* where was a fine article on the illnesses and deaths of the Presidents. Now with Mistress Pepys to the Public Library where assembled some 30 Chicago authors who had written books this year. Six were clerics involved in theological questions, a half-dozen were elderly women involved in tales for tiny tots, Judge Braude had another great collection of anecdotes and witticisms, and Melanie Pflaum and Lois Stern had novels. After that to shop and to Andy's Epicurean Cafe—the king of strudel—for beef goulash with *spaetzle*, and then to a great gathering for La Rabida at the Congress with Albert Pick presiding. The movie was a hilarious story of an Army hospital in France with Ernie Kovacs and Mickey Rooney called "Operation Mad Ball."

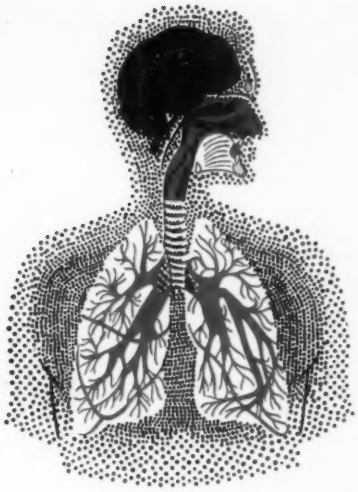
Dec. 6—At the scrivening and in the evening to the Cook County Hospital where Arthur Bowes showed the pictures of his trip through Russia. Dan Ryan spoke for the Hektoen Institute and the intake of spirits raised spirits and cash for research. So read a slow-going mystery by Craig Rice called "Knocked for a Loop," and the British ladies who ladle out the mysteries do better than the Americans.

Dec. 7—Editing manuscripts for a new book and in the afternoon watching Pittsburgh and New York splattering in the mud, and began to wonder at the psychology of the enjoyment of either patrons or players.

Dec. 8—To pick up Joseph Schildkraut at the Ambassador West and took him to Sinai Temple where he held some thousands enthralled with the story of the background of Anne Frank's diary. Then come Schildkrauts, Manns, Kirsners, Winstons, Maurice Goldblatt and the Martins to dinner. Thereafter to Soroko's Revlon cocktail party at the Palmer House, meeting the Clyde Cummers from Cleveland, Rudolph Baer, Cunningham of San Diego, Naomi Karnof of the District of Columbia, Goldberg of Cincinnati and dermatologists from everywhere. Then with all the family to see again the Anne Frank play and took them all to Fritzel's for dinner where Mike Todd and Elizabeth Taylor were dining with the Kupcinets.

Dec. 9—Up betimes and at noon to the Chicago Heart Ass'n.

(Continued on page A-166)



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where Wright Adams, Oglesby Paul, Pete Talso, Walter Priest and all the staff discussed problems of public education. Then to the Academy of Dermatology to view the exhibits. In the evening to dine at the Blackstone and heard A. Sachar, president of Brandeis, Scharfman and Jack Goldfarb, who gave a million dollars for a library, give inspiring addresses.

Dec. 10—At "The Bath" in the Ambassador as guest of Pat Hoy and his lovely lady for the annual meeting of the Board of the Municipal Tuberculosis Sanitarium. Here were Mayor Daley, Bundesen, Irons, de Young, Bialis, Si Moore, Hutton, Lichtenstein, Levine and all the staff. Irons rendered a fine report and a method was found to use the beds at the Chicago State Hospital. Levine in a lengthy disquisition found many faults with so many aspects that old Pepys was reminded of the lady watching the parade. She said to her husband: "Look, John, they are all out of step but Jim." Thereafter Hutton and old Pepys drove homeward with Bundesen who kept talking on his motorcar telephone to sundry numbers.

Dec. 11—By the morning plane to New York which is tortured with a subway strike. En route read a novel of Storm Jameson's called "A Cup of Tea for Mr. Thorgill," telling of Oxford University and revolving around trouble with the young people seduced by communism, and I did not know they were so much involved. In the afternoon to conferences at Doubleday's and then came Mel Evans and the Milton Lasdons. After dining, to see a play by Morton Wishengrad called "The Rope Dancers" which is full of psychologic implications and superstitions. Here the acting of Art Carney, Joan Blondell, Siobhan McKenna and, particularly, Theodore Bikel as a family doctor was scintillating.

Dec. 12—Driving early with Bill and Stanley Lasdon to Morris Plains, N. J., and there a fine luncheon with Bobst, Driscoll and Scheele and conferred until late in the afternoon. Then for dinner came Otto Frank, father of Anne Frank, his lady and the Bill Lasdons, and all were fascinated to hear details of Frank's great tragedy.

Dec. 13—Up betimes for breakfast with Art Schendorf and an interview on medicine; next to the shops and to see Herb Mayes at *Good Housekeeping*. Thereafter to confer with Bobst, Driscoll, Lasdon, Robinson and Peter Warren at the Metropolitan Club. In the evening with Basil O'Connor and his charming Hazel to dine on wonderful beef at the Little Club and tried the seafood cocktail and the *soufflé* dessert. Then to see "Fair Game" with Sam Levene, which is great fun, and to the Stork Club to meet Herbert and Grace Mayes and saw Billingsley, Bert Lahr and Bob Considine, but somewhere in the excitement the coat-check girl gave somebody else Basil O'Connor's coat.

Dec. 14—Back to Chicago by the airplane—a fine flight—meeting Bob Buerki en route to Detroit as we landed. And all the afternoon and evening talking to the Dictaphone.

Dec. 15—Conferring with Justin on the editing. In the afternoon with Maurice Goldblatt to see the new Friend Pavilion for convalescence and rehabilitation at Michael Reese. Here were Grant Pick, Hollender, Turner, Robert Levy, Jay Herz and many more. The pavilion provides beds and divisions for occupational and physical therapy.

Dec. 16—For a conference came Sylvia Covet and to luncheon with her and Z. W., and we figured out new features for POSTGRADUATE MEDICINE. In the late afternoon with Joe Kirsner and the ladies to the Tavern, dining sumptuously, and then for the benefit of the English Speaking Union to see the Royal Ballet in "The Sleeping Beauty."

Dec. 17—Today came 22 girls handicapped by poliomyelitis, cerebral palsy and amputations whom Mistress Pepys entertains each year, for well-nigh 25 years now, giving them a Christmas party and gifts and arranging for their coming and going. And with this her face glows with her delight in the doing.

Dec. 18—By the morning plane to New York, reading en route "Not by Bread Alone," the Russian novel by Dudinskov which is widely discussed. At noon came Mel Evans to discuss literary projects. Thereafter to confer at Doubleday's and then to the City Hall to participate in a legislative hearing on "Care of the Aged." First, A. A. Berle of the American Molasses Company and the Twentieth Century Fund spoke of pension plans and presented two satellites who are his advisers. Next, Senator Desmond introduced Senator Johnson, son of my old friend of many years in Batavia, and he introduced old Pepys. In the evening with the Evans and Beebes to an Italian restaurant on West 46th Street to eat broiled scampi in the shells and *spumone*.

(Continued on page A-168)

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Dec. 19—Up for breakfast with James Troupin, discussing medical affairs; thereafter visiting Macy's and other emporiums. At noon to the Metropolitan Club for luncheon with Bobst, Driscoll, Lasdon, Scheele, Warren, Robinson, Williams and Fossil; then out to Idlewild.

Dec. 20—All this day intensely engaged with the periodicals and the scrivening and heard from Z. W. of her consent to marry a teacher of English, which should be the fate of every Girl Friday.

Dec. 21—To the Holy Name Cathedral where Cardinal Stritch conducted a mass and memorialized the services of John B. Murphy, great surgeon, on the hundredth anniversary of his birth, for some hundreds of people. Thereafter to a breakfast in the John B. Murphy Memorial of the American College of Surgeons, meeting our hostesses, the daughters, Mrs. James Edward Baggott, Jr., Mrs. Edward Nash Hurley and Mrs. Andrew Edwin Van Esso, the children and the grandchildren—and among them none going into medicine. Here met I. Ravdin who flew in from Philadelphia, Paul Hawley, the Dragstedts, O'Donoghues, Theobalds, Karl Meyer, McNealys, and reflecting sadly how many of the famed of Murphy's period are now gone.

In the afternoon took to bed with what is called virus enterocolitis but still somewhat suspicious of the broiled scampi.

Dec. 22—In bed and watched the Lions and the Forty-niners which was a great show with the Lions coming from behind in a dazzling display of football feats. Read meanwhile a novel of suspense by Nicholas Blake called "End of Chapter," an intricate machine-made plot of murder in a publishing house.

Dec. 23—Canceling engagements, entertainments and enterprises and convalescing pleasantly in the midst of an avalanche of mail. The Christmas cards come in by hundreds and with them many letters bespeaking pleasure in the diary which greatly gladden the hearts of old Pepys and his lady. Here a fond note from Roger Lee, a warm appreciation by David Allman, notes from Edith Bulson, Susie West, Mary Switzer, Clemmesens, Orskov, Bill Frohlich, Elmer Bobst, Robert Peers, and many, many more who all are dear to us. And now reading the first novel ever I have read about a pharmaceutical detail man. "The Medlars," written by Herbert Silvette, is a parody of the third book of Rabelais; Silvette is professor of theoretical pharmacology in the Medical College of Virginia.

Dec. 24—Busy with preparations for Christmas Day and unable to make the usual round of festivities in the clubs where many gathered to "imbibe spirituous liquors in their blood." Did, however, convene as usual at the Lying-In Hospital where came Hesseltine, Dorfman, Mesdames Wanzer, Hopkins and Koff and nurses Kirchner and Mitchell.

Dec. 25—A great holiday and there came the Schildkrauts, the Hoffmans and all the Markses and Justin's family and Merriel and Morris Friedell, and the dinner was delightful. From Schildkraut came a first edition of Samuel Pepys' Diary which is a wonderful acquisition for the library, this one in two massive leather-covered volumes and originally owned by the Marquis of Stafford.

Dec. 26—Post-Christmas thank-you letters and embarking at the desk on several new literary ventures. Read too a novel of menace by Selwyn Jepson who wrote "The Assassin." In "A Noise in the Night" he has a story of Algerian intrigue—high quality in the overabundant mystery field.

Dec. 27—Engrossed with the periodicals, lay and medical, and all reaching such a high state of perfection as to demand hours of time for their perusal.

In the evening to the Tavern for a farewell dinner to the Schildkrauts with Judge Brown and his lady and the Winstons.

Dec. 29—In the afternoon to a reception at my nephew's, Dick Fishbein, and saw great numbers of grandnieces and grandnephews to the point of being startled by their profusion. Watched an inspired team, the Detroit Lions, win the professional football championship from the Cleveland Browns who could not do anything right. In the evening took the teen-agers to dine at the Standard Club and to hear and see Tchaikovsky's "Swan Lake."

Dec. 30—At noon come John Mentzer with Mesdames Brown, Frieder, Wolfson and Richards to luncheon and to present to old Pepys for La Rabida a check for $15,000 from the Children's Aid, all realized by their Christmas card project.

Dec. 31—Now come the end of 1957, so sat at home watching "The $64,000 Question" on television and the merrymakers at midnight in various places whom television brought to us.